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ABSTRACTS OF WORLD MEDICINE

It is the aim of this journal to provide the reader with abstracts of all important articles appearing in medical periodicals published in every part of the world, and in this way to enable him to keep in touch with new developments throughout the whole field of medicine and in each of its special branches, including those aspects of surgery which are of particular concern to the physician.

More than 1,600 periodicals are surveyed, from which are selected for abstracting those papers which appear to make some useful contribution to the sum of medical knowledge or experience. Each paper is abstracted in sufficient detail to indicate to the general reader the nature and value of that contribution and to enable the specialist to assess its importance in relation to his own work and to decide whether the original article should be read in full. The author's own summary or an editorial summary published with the original article may occasionally be reproduced if it is suitable for these purposes, and the title and reference alone may be published in order to draw attention to a review article or other type of paper which cannot readily be abstracted.

The abstracts in each issue are grouped in sections according to subject and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together. The titles of papers written in languages other than English are given both in translation and in the original form. The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals*, as modified by *ISO Recommendation R4: International Code for the Abbreviation of Titles of Periodicals* (International Standards Organization, 1957), and in *World Medical Periodicals* (Second Edition, World Medical Association, 1957). The transliteration of authors' names from the Cyrillic alphabets is in accordance with *ISO Recommendation R9: International System for the Transliteration of Cyrillic Characters* (International Standards Organization, 1955).

Explanatory or critical comments by the abstracter or editor are enclosed within square brackets.

ABSTRACTS OF WORLD MEDICINE

VOL. 29 NO. 4 APRIL, 1961

Pathology

634. **Pancreatic Damage Induced by Excess Methionine**
N. KAUFMAN, J. V. KLAVINS, and T. D. KINNEY. *Archives of Pathology* [*Arch. Path.*] **70**, 331–337, Sept., 1960. 4 figs., 26 refs.

It has been known for 10 years that ethionine, the non-methylated analogue of methionine, can damage the liver and pancreas when fed to experimental animals. Animal experiments at Western Reserve University, Cleveland, Ohio, have shown that methionine similarly damages the pancreas, but not the liver. Two groups of albino male rats were fed diets containing 18% protein supplemented with 2% and 4% methionine respectively, while 2 pair-fed control groups received the basal diet alone. A further group was fed the basal diet *ad libitum* and a sixth group the basal diet in limited amounts. All the animals were killed after 30 days and the pancreas and liver examined histologically. There was extensive damage to the acinar cells of the pancreas in all the rats receiving methionine supplements. In the pair-fed controls and the rats fed *ad libitum* the pancreas was histologically normal, whereas in the group given the restricted diet there were varying degrees of loss of cytoplasmic basophilia of the acinar cells, but to a much smaller extent than in those given methionine. The livers of the rats fed methionine were essentially normal, in contrast to the findings when ethionine is given.

H. Lehmann

635. **Nephrocalcinosis: Electron Microscopical Findings in Experimental Studies.** (Sur la néphrocalcinose: recherches expérimentales au microscope électronique)
A. POLICARD, A. COLLET, H. DANIEL-MOUSSARD, and S. PREGERMAIN. *Presse médicale* [*Presse méd.*] **68**, 1735–1738, Oct. 26, 1960. 6 figs., 23 refs.

Nephrocalcinosis was experimentally produced in rats by the intraperitoneal injection of 1·5 ml. of a 10% solution of calcium gluconate daily for 9 days. The animals were then killed, the kidneys fixed, and the lesions examined under the ordinary and electron microscopes. Two distinct types of calcium deposit were found; one, which was beyond the power of resolution of the light microscope, consisted of crescent-shaped bundles which were localized in Bowman's membrane, the parietal cells of the glomeruli, and the cells of the proximal renal tubules. The other type of deposit was large enough to be visible by the ordinary microscope and was found in thin concentric layers in the basement membrane of the renal tubules. Calcium deposits were particularly common in the cytoplasm of connective-tissue cells, but they were not seen in intracellular vacuoles or in mitochondria in these cells, though deposits did occur around these structures. It was particularly noted that there were no calcium deposits within collagen fibres.

G. W. Csonka

636. **Electron Microscopical Appearances in the Kidney after Experimental Ligation of the Jejunum: a Contribution to the Morphogenesis of Acute Nephrosis.** (Elektronenmikroskopische Nierenbefunde nach experimenteller Unterbindung des Jejunum: ein Beitrag zur Morphogenese der akuten Nephrose)
H. J. LÖBLICH and C. SCHÖRCHER. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **333**, 356–367, 1960. 3 figs., 26 refs.

In order to demonstrate the electron-microscopic changes in the early stages of acute renal damage the jejunum of 12 white mice was ligated. Twenty-four hours after the ligation the glomerular capillaries were found to be widely dilated, the endothelial and epithelial cells swollen, and the middle zone of the basement membrane and the microvilli of the epithelial cells greatly widened. The epithelial cells of the proximal convoluted tubules revealed apical oedema of their cytoplasm and enlarged mitochondria, with an increased storage of osmiophilic substances. At 48 hours the changes in the glomeruli had increased quantitatively. In the epithelial cells of the proximal convoluted tubules a basal oedema of the cytoplasm could be demonstrated, as well as a swelling of the mitochondria (with preserved cristae), a widening of the extracellular spaces, broadening of the basement membrane, and an intense oedema of the endothelial cells. The structure of normal kidneys of mice were used as controls. The most important factor in the pathogenesis of the acute renal damage seemed to be the change in pressure resulting from the acute circulatory disturbances in the nephron.—[From the authors' summary.]

637. **Megaloblastic Erythropoiesis in Pregnancy**
A. MACKENZIE and J. ABBOTT. *British Medical Journal* [*Brit. med. J.*] **2**, 1114–1116, Oct. 15, 1960. 3 figs., 22 refs.

Anaemia of pregnancy is undoubtedly due in most cases to iron deficiency, but there is a growing volume of evidence that in many cases the anaemia is megaloblastic in type, due most probably to deficiency of folic acid, either from inadequate dietary intake or poor absorp-

tion. The incidence of megaloblastic erythropoiesis was studied in all patients admitted over a 12-month period to Sunderland Maternity Hospital. For this purpose the haemoglobin level was estimated and stained blood films were examined, and in those cases in which blood films revealed abnormality marrow biopsy smears were obtained (at least 4 in each case) and stained by the May–Grünwald–Giemsa or the Leishman technique; aspirated marrow fragments were stained with haemalum and eosin and also for iron. The incidence of megaloblastic erythropoiesis was one in 26·6 deliveries and one n 4·2 twin deliveries.

Of the 95 marrow biopsies, 73 showed megaloblastic erythropoiesis, unequivocal megaloblasts usually being associated with severe anaemia (73% of the patients had a haemoglobin level of 7 to 10 g. per 100 ml.), but in some cases with only a slight degree of anaemia. Transitional type erythropoiesis was also present in association with a sufficiency or a deficiency of iron. Megaloblastic anaemia tended to develop more readily in patients in the older age groups than in those in the younger. As regards complications, of 68 cases of which details were available, antepartum haemorrhage occurred in 4 (6%) compared with an over-all incidence in the unit of 2·7%; some degree of pre-eclamptic toxaemia was observed in 29 (42·5%) compared with 12·7% in the unit. It is considered that folic-acid deficiency is the probable cause of megaloblastic erythropoiesis and may aggravate some obstetrical complications. Although the haemoglobin level in patients with pre-eclamptic toxaemia was not different from that in patients without toxaemia, the association between megaloblastic erythropoiesis and toxaemia is close enough to merit further study.

Ethel Browning

638. **Radiochromium in the Estimation of Survival of Red Blood Cells: Review of the Literature**
A. C. AUFDERHEIDE. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **34**, 258–267, Sept., 1960. Bibliography.

639. **Squamous Cell Nests of the Pituitary Gland as Related to the Origin of Craniopharyngiomas: a Study of Their Presence in the Newborn and Infants up to Age Four**
G. M. GOLDBERG and D. E. ESHBAUGH. *Archives of Pathology* [*Arch. Path.*] **70**, 293–299, Sept., 1960. 8 figs., 14 refs.

Because of the failure to find structures in the region of the pituitary that could be interpreted as developmental cell nests from the craniopharyngeal recess (Rathke's pouch) in subjects under the age of 20 years some doubt has been cast on the theory that it is from these that craniopharyngiomata arise. With a view to discovering whether such cell nests do in fact occur in the young the authors have examined the pituitary stalk in 128 infants and children up to 4 years of age who had come to necropsy at the Michael Reese and Cook County Hospitals, Chicago. In 4 of the infants they found cell clusters resembling embryonal remnants, and they suggest that this finding supports the above theory of the origin of craniopharyngiomata. *J. B. Cavanagh*

640. **Recent Studies in the Immunology of Cancer. V. Detection of Tumors in Man by the Skin Testing of Polysaccharide–Antibody Complexes**
J. G. MAKARI. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **8**, 675–688, Sept., 1960. 3 figs., 13 refs.

The author, at Muhlenberg Hospital, Plainfield, New Jersey, has further elaborated a diagnostic test for cancer. Polysaccharide-like materials extracted from tumours were mixed with the patient's trypsinized serum and injected intradermally. The diameter of the resulting erythematous area was compared with that resulting from injection of serum alone. The test was regarded as positive if the ratio of diameters was 1·4 or more, and negative if it was 1·2 or less. Among 35 patients with carcinoma the test was positive in 27, doubtful in 7, and negative in 1. Of 12 patients with benign tumours the test was positive in 6, doubtful in 4, and negative in 2; and in 111 patients with other diseases or "volunteers" [presumably this means normal individuals] there were 21 positive, 22 doubtful, and 68 negative results.

[There appears to be something here of potential interest to cancer research workers, but unfortunately the author has so closely interwoven experimental results with special pleading and rather free speculation that many workers may not have the patience to separate them.]

M. C. Berenbaum

CHEMICAL PATHOLOGY

641. **Electrophoretic Partition of Cerebrospinal Fluid and Serum Proteins in Multiple Sclerosis**
D. BRONSKY, S. E. KAPLITZ, J. MUCI, A. DUBIN, and E. J. CHESROW. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **56**, 382–390. Sept., 1960. 43 refs.

The authors compare the electrophoretic patterns of serum and cerebrospinal-fluid (C.S.F.) proteins from healthy subjects with those from patients with disseminated sclerosis. They have been enabled to do this effectively even when C.S.F. proteins were in low concentration by concentrating them up to fiftyfold by dialysis against 20% polyvinylpyrrolidone. They found that the serum and C.S.F. proteins behaved electrophoretically in an identical manner. The partition of serum proteins from patients with disseminated sclerosis did not differ from normal. Patients whose C.S.F. gave an abnormal colloidal-gold curve showed a highly significant increase in the γ-globulin and fall in the albumin fraction of C.S.F. proteins. Patients with a normal colloidal-gold curve, however, showed only a significant decrease in the β-globulin fraction.

Out of the 23 patients examined, only 4 had an abnormal colloidal-gold curve. In general, these had a more active and earlier disease process than those with normal gold curves. The raised γ-globulin content of the C.S.F. of the former is attributed by the authors to the occurrence of plasma cells in relation to recently formed areas of demyelination. In their discussion they review other viewpoints regarding the origins of this protein fraction. *J. B. Cavanagh*

642. **A Test of Thyroid Function Using an Extract of Posterior Lobe of the Pituitary Gland.** (L'épreuve à la post-hypophyse dans l'exploration de la fonction thyroïdienne)
—. Gilbert-Dreyfus, J. C. Savoie, E. Bernard-Weil, and J. Sebaoun. *Presse médicale* [*Presse méd.*] **68**, 1647–1650, Oct. 15, 1960. 8 figs., 21 refs.

The authors have developed, and here describe, a test which, they claim, helps to distinguish between the types of hypothyroidism due to failure of the action of thyrotrophic anterior pituitary hormone. In this test an intravenous injection of 5 units of posterior pituitary extract or 5 units of synthetic oxytocin is given daily for 3 successive days. This causes a rise in the curve of uptake of radioactive iodine (^{131}I) by the thyroid gland in patients who had previously given a low ^{131}I uptake curve. They consider that this result suggests that thyrotrophic hormone can be secreted by the anterior lobe of the pituitary gland in response to stimulation by neuro-hormones originating in the diencephalon. If the anterior pituitary lobe is in a resting state because of the absence of hypothalamic excitation the injection of oxytocin will stimulate the secretion of thyrotrophic hormone—an action which can be detected by the rise in uptake of ^{131}I by the thyroid gland. However, if the hypothyroidism is secondary to destruction of the anterior lobe of the pituitary the result of the oxytocin test will be negative. This contrasts with the positive effect of administration of thyrotrophic hormone in all cases of hypothyroidism not due to lesions of the thyroid gland itself. These experiments also suggest that there is a neuro-hormonal substance chemically related to oxytocin.
M. C. G. Israëls

643. **Significance of the Glycogen Content of the Neutrophil Granulocytes in Health and Disease.** (О значении содержания гликогена в нейтрофилах)
B. A. Pavlov. *Терапевтический Архив* [*Ter. Arh.*] **32**, 44–48, Sept., 1960. 1 fig., 23 refs.

Since little is known about the variations in the glycogen content of neutrophil granulocytes in different physiological and pathological conditions the author has examined 218 blood films and 35 bone-marrow smears from patients with various conditions, using a modification of the staining method of Shabadash. Phagocytic activity and cell motility were also studied by phase-contrast microscopy.

Large amounts of glycogen were demonstrated in the neutrophil granulocytes of 20 healthy subjects aged 18 to 40 years, while smaller amounts were found in the eosinophils, monocytes, and lymphocytes. In 15 bone-marrow smears from healthy controls glycogen was scarce in the young neutrophil elements, but its concentration increased *pari passu* with maturation. No change in the glycogen content of neutrophils was observed in 17 athletes after major physical effort, in 5 healthy controls after ingestion of food, in 10 patients with hypertension and various neuroses, in 10 patients with thyrotoxicosis, or in patients with hepatic cirrhosis. A rise in the neutrophil glycogen content was demonstrated in diabetics with a blood sugar level over 200 mg. per 100 ml. and receiving more than 50 units of insulin daily. It seemed that the proportion of intensely or moderately stained cells increased with the dose of insulin, but no direct relationship could be demonstrated between glycogen content of the cells and blood sugar levels and no significant change occurred after ingestion of 100 g. of glucose. A marked rise in the glycogen content was observed at the onset of acute inflammatory processes in 22 out of 25 patients with a leucocytosis of over 11,000 per c.mm. A return to normal content accompanied resolution. Increased glycogen content was associated with increased motility of the cells.

A considerable reduction in the neutrophil glycogen content was observed in 20 of 26 patients with hypoplastic blood diseases, the process of loss of glycogen becoming apparent at a relatively early stage of development of the neutrophil granulocyte series in the bone marrow. In a majority of 25 patients with chronic leukaemia a reduction in glycogen content was also associated with diminished motility of the cells. In exacerbations of chronic reticulosis and lymphadenosis up to 70% of the lymphocytes and lymphoreticulocytes contained peripheral glycogen granules. In infectious mononucleosis the glycogen content was normal, but in a majority of 25 patients with rheumatoid arthritis or bronchial asthma treated with ACTH (corticotrophin) it was reduced and there was an increase in the alkaline-phosphatase concentration, thus confirming the connexion between these two values previously reported. It is concluded: (1) that the synthesis of glycogen takes place in the neutrophil polynuclear granulocytes themselves, with alkaline phosphatase playing a definite role in the process; (2) that glycogen is not merely transported by those cells, but is essential for their functional activity; and (3) that there is a close relationship between the glycogen content of the neutrophils and their phagocytic activity.
S. W. Waydenfeld

644. **A New Method for Determination of Potassium in Serum**
E. Bladh and P. O. Gedda. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **12**, 274–276, 1960. 2 figs., 1 ref.

A new method of estimating the serum potassium level, based on the reaction between potassium and sodium tetraphenylborate in which the very sparingly soluble compound potassium tetraphenylborate is formed, is described in this paper from the University Hospital, Lund, Sweden.

The serum protein is first precipitated with trichloracetic acid and the sample centrifuged; then to the clear supernatant excess sodium tetraphenylborate is added. The precipitate of potassium tetraphenylborate is centrifuged and the excess of sodium tetraphenylborate is titrated turbidometrically with a quaternary ammonium salt, cetyltrimethyl ammonium bromide (C.T.A.B.). [The reagents and apparatus are listed; the method is that previously described by Karman *et al.* (*Mikrochim. Acta* (*Wien*), 1959, **5**, 779).] Pure potassium salt solutions of known concentration are used to construct a calibration curve with the amount of potassium in μg.

per 0·1-ml. sample as ordinate and the amount of C.T.A.B. (difference between the amount consumed by a blank and by the sample in question) as abscissa. This graph is a straight line passing through the origin. The reproducibility of the results is demonstrated in a table giving the values of 3 parallel estimations on each of 4 samples and on the blank, there being little variation in the figures obtained.

The serum potassium level in 20 patients with rheumatoid arthritis was determined by this method and also by flame photometry. There was good agreement between the results of the two methods, the slightly higher values obtained by the new method being attributed to the absence of protein in the sample analysed.

The authors consider that their method "is not as rapid and uncomplicated as the flame photometric determination, but it seems to be useful as an alternative".

I. Berkinshaw-Smith

645. **Biological Changes in Delirium Tremens.** (Le syndrome biologique du délirium tremens)
G. Boudin, A. Lauras, M. Laniècе, and H. Krebs. *Presse médicale* [*Presse méd.*] **68**, 1469–1472, Sept. 17, 1960, and 1503–1506, Sept. 24, 1960. 1 fig., 39 refs.

The authors report the results of biochemical investigations carried out on 115 patients with delirium tremens, of whom 110 were in crisis at the time of investigation. There were 11 deaths. All the patients were rehydrated by mouth, as far as possible, during the investigation. Most of them were chronic wine drinkers with a history of alcoholism of 10 years or more and the crisis was preceded in most cases by a febrile infection or trauma.

The characteristic biochemical findings were as follows. A negative potassium balance (a low serum level and high urinary excretion of potassium), a normal sodium balance, normal calcium levels in the blood and urine, a low serum magnesium level, a low serum chloride level rapidly becoming normal on treatment, reduced alkali reserve, marked ketonuria, an increased blood urea level reaching a peak of about 60 mg. per 100 ml. on the third day of the crisis, and increased urinary excretion of urea, phosphate, and uric acid. As the crisis resolved the blood and urine values became normal. The authors suggest that these metabolic changes are due to powerful stimulation of the adrenal cortex by whatever is responsible for producing the attack of delirium tremens and are not in themselves the cause of the crisis.

The blood ammonia concentration was studied in 10 patients during the crisis. At the peak of the patient's confusion this level was slightly raised in 7 patients, but there was no correlation between the level and the degree of confusion. However, it was noted that the blood ammonia level varied with the blood urea level. Renal function tests gave normal results except for some transient albuminuria. The results of liver function tests were abnormal in about 90% of cases; in most of these the results of empirical tests were positive and the serum γ-globulin level raised. Clinically, 69% of the patients had hepatomegaly and 3% cirrhosis with jaundice. The eosinophil count fell to less than 40 per c.mm. after the first day, but slowly rose to normal during convalescence.

M. Lubran

646. **Copper Content of Organs of Patients with Hepatolenticular Degeneration.** (Содержание меди в тканях больных гепато-лентикулярной дегенерацией)
L. K. Bauman. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 1141–1145, No. 9, 1960. 12 refs.

It is well known that in hepatolenticular degeneration there is retention of copper in the blood and increased excretion of the metal in the urine, and also that many of the organs contain several times the normal amount of this element. In the study here reported the organs of 3 patients who died of the disease were analysed and these facts confirmed. The highest values (presented in μg. per g. dried tissue) were obtained in the liver, the frontal lobes and paracentral gyrus of the brain, the occipital lobe, caudate nucleus, and basal ganglia, especially the globus pallidus. The kidneys contained much less copper (less then one-third of the content of the above organs) and the adrenal glands and spleen still less. The value for the smooth muscle of the small intestine was more than double that for heart muscle and over three times that for the rectus muscle of the abdomen; only traces were found in the rectus femoris.

Each of the 3 patients suffered from a different type of the disease, one having the pyramido-cortical type, one the infantile type, and one the type characterized by rigidity and tremor. There was no significant difference in the distribution of copper in the tissues [but from the data presented there appears to have been more copper in the liver and less in the caudate nucleus of the patient with the infantile type]. The blood copper level was normal in all 3 cases, while urinary excretion was normal in one but raised in the other 2 to 2 to 3 times the normal value; in one of these last it rose during an attack of erysipelas to 10 times the maximum normal value. The excretion of amino-acids in the urine was normal in 2 patients and slightly raised in one. In one of the former —the child who developed erysipelas—the urinary amino-acid excretion rose to 800 mg. in 24 hours.

L. Firman-Edwards

647. **Electrolyte Metabolism and Aldosterone Secretion in Benign and Malignant Hypertension**
J. H. Laragh, S. Ulick, V. Januszewicz, W. G. Kelly, and S. Lieberman. *Annals of Internal Medicine* [*Ann. intern. Med.*] **53**, 259–272, Aug. [received Oct.], 1960. 7 figs., 22 refs.

A new technique for measuring the amount of aldosterone secreted by the adrenal glands has been developed at Columbia University, New York, and used in studying the relationship between aldosterone and hypertension. A tracer of tritium-labelled aldosterone was injected and the specific activity of the tetrahydroaldosterone in the subsequent 24-hour specimen of urine determined. The difference between the specific activity of the tracer and that of the metabolite was taken as a measure of the endogenous contribution.

Secretion rates in 2 patients with benign hypotension were respectively 250 μg. and 330 μg. per day—values within the normal range. Sodium deprivation resulted in a prompt reduction in renal sodium secretion and a

rise in aldosterone secretion (up to 930 μg. and 580 μg. per day). No significant change in blood pressure was noted at the time. Another patient with benign hypertension showed no change in aldosterone secretion during sodium deprivation until potassium was administered. The aldosterone response to sodium deprivation is apparently dependent upon the state of the potassium balance. These levels and responses are similar to those found in healthy subjects under similar circumstances.

Studies were also undertaken on 6 patients with malignant hypertension. All 6 patients had a diastolic pressure higher than 130 mm. Hg and all showed evidence of nitrogen retention. The plasma level of potassium tended to be low and of bicarbonate high. There was hypersecretion of aldosterone in each case, ranging from 600 to 10,000 μg. per day. Necropsy in all cases revealed moderate bilateral hyperplasia of the adrenal glands with increased lipid content, but no adenoma.

In 2 further patients with severe hypertension the greatly increased rate of secretion of aldosterone could not be influenced by changes in sodium intake. Potassium repletion without sodium restriction in another patient suffering from severe hypertension resulted in a rise in aldosterone secretion from 1,200 μg. to 2,700 μg. per day.

It appears that severe and malignant hypertension differ from the healthy state and from benign hypertension in the amount of aldosterone secreted and in the response to sodium depletion. Excess aldosterone leads not only to hypertension, but also to potassium depletion and sodium retention. In 16 patients with malignant hypertension the average plasma concentration of potassium was 3·6 mEq. per litre and of bicarbonate 29 mEq. per litre.

A chart is included in which the daily aldosterone secretion of 46 patients is compared. This shows that only those patients with primary aldosteronism, advanced hypertension, and malignant hypertension had an increased rate of secretion, while those with benign hypertension and unilateral renal disease had a normal rate.

G. Clayton

648. **Catecholamines in Patients with Pheochromocytoma**

J. L. Bollman, E. V. Flock, G. M. Roth, and W. F. Kvale. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **56**, 506–519, Oct., 1960. 2 figs., 39 refs.

The concentration of the catechol amines, adrenaline and noradrenaline, in blood, urine, and tumour tissue from 48 patients with phaeochromocytoma has been measured by various fluorometric methods at the Mayo Clinic, Rochester, Minnesota. The clinical value of such estimations in the blood and urine as a test for phaeochromocytoma is discussed.

The catechol amine concentration was usually considerably greater in phaeochromocytoma tissue (0·3 to 17·5 mg. per g.) than in the adrenal gland (0·10 to 0·75 mg. per g.). The concentration in urine and plasma from patients with phaeochromocytoma was higher than normal, either continuously or intermittently, because of release from the tumour; the 24-hour urinary output of catechol amine ranged from 317 to 2,780 μg. (normal, 10 to 643 μg.) and the plasma level from 6·0 to 86·5 μg. per litre (normal, about 2·4 μg. per litre). Hingerty's qualitative test (*Lancet*, 1957, **1**, 766; *Abstr. Wld Med.*, 1957, **22**, 126) is recommended for the rapid screening of 24-hour specimens of urine when the tumour is actively secreting catechol amines. Sobel and Henry's quantitative procedure (*Amer. J. clin. Path.*, 1957, **27**, 240) provides additional information on the total amount of catechol amine in hydrolysed urine. Medication with salicylates and other drugs that produce fluorescence must be avoided. Measurements of plasma level by Weil-Malherbe and Bone's method (*Biochem. J.*, 1952, **51**, 311) frequently provides additional diagnostic information. When the tumour was either small or not actively secreting catechol amines chemical testing for phaeochromocytoma was positive only on blood withdrawn either during a spontaneous attack of paroxysmal hypertension or during an attack provoked by a histamine injection. The amount of catechol amine found in blood and urine did not give an accurate indication of the amount stored in the phaeochromocytomata.

J. E. Page

649. **Catecholamines and the Diagnosis of Pheochromocytoma: a Review and Evaluation**

R. Straus and M. Wurm. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **34**, 403–425, Nov., 1960. 3 figs., bibliography.

650. **A Hormone Inhibiting Cholecystokinin. Its Role in Biliary and Pancreatic Disorders.** (L'hormone inhibitrice de la cholécystokinine. Son rôle en pathologie biliare et pancréatique)

J. Caroli, J. Plessier, and B. Plessier. *Revue française d'études cliniques et biologiques* [*Rev. franç. Et. clin. biol.*] **5**, 545–557, June–July, 1960. 12 figs., 17 refs.

It has been shown that the muscular activity of the gall-bladder and of the sphincter of Oddi is regulated by a double hormone control, motility being controlled not simply by the endogenous hormone cholecystokinin described by Ivy (*Amer. J. Physiol.*, 1930, **91**, 336, and *Physiol. Rev.*, 1934, **14**, 1), but also by a second hormone which acts as an inhibitor of the endogenous hormone. Urinary cholecystokinin can be estimated in man by the method of Svatos (*Nature* (*Lond.*), 1959, **129**, 567), while the second, inhibitory, hormone is estimated either by bio-assay (inhibition of the action of the purified cholecystokinin preparation of Jorpes and Mutt on gall-bladder contraction (*Nord. Med.*, 1956, **56**, 1511)), or by paper electrophoresis.

This anti-hormone is considered to play a fundamental role in bile-duct physiology, and an excess of it could explain cholecystatonic states. The authors state that "an excessively rapid fall [in the level of the anti-hormone] after fatty meals could precipitate acute pancreatitis or its relapse". The anti-cholecystokinin, it is suggested, is probably secreted by the gall-bladder wall rather than in the duodeno-jejunal region.

L. A. Elson

Microbiology and Parasitology

651. **Comparison of a BSh Strain of *Leptospira* from a Swamp Near Moscow and Related to Free-living Leptospires, with *Lept. semarang*, the Pathogenic Strain Isolated from a Rat in Indonesia.** (Сравнительное изучение выделенного из болота Московской области штамма БШ, относящегося к свободно живущим лептоспирам, и патогенного штамма Semarang, выделенного от крысы в Индонезии)
V. I. Terskih. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Ž. Mikrobiol. (Mosk.)*] **31**, 48–53, Sept., 1960. 12 refs.

In 1956 Broom, of the Wellcome Laboratories of Tropical Medicine, London, drew the attention of the present author to the fact that leptospire strains described in the U.S.S.R. as "BSh" strains were serologically identical with *Leptospira semarang*. After an exchange of strains and antisera this has now been confirmed in Moscow.

Since 1933 agglutinating antibodies against the BSh strains and *Lept. semarang* have been demonstrated frequently in sera from patients in various regions of the U.S.S.R., Java, and India, with titres ranging from 1:400 to 1:20,000. Isolations of similar leptospiral strains, from patients as well as from rats, have been reported repeatedly in the U.S.S.R. Furthermore, in 1955 and 1956 leptospires were isolated from the kidneys of *Spermophilus* (a kind of marmot) and swine in Roumania which showed a close serological relationship to *Lept. biflexa*. This species in turn was found to be related to *Lept. semarang* and *Lept. madida*. The sera of a considerable number of patients in Roumania were found to agglutinate to *Lept. biflexa*, and Roumanian authors consider that *Lept. biflexa* possesses a general leptospiral antigen.

In the light of the present author's recent work it would appear that *Lept. semarang* and the BSh strains, which by now have been maintained for many years in laboratory media, are really modified strains of *Lept. biflexa*. It would be important to shed more light on the pathogenicity of free-living *Lept. biflexa* for man and animals. *K. Zinnemann*

652. **Studies in Tuberculo-immunity**
H. S. Willis, H. M. Vandiviere, M. R. Vandiviere, and I. Melvin. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **240**, 137–158, Aug., 1960. 17 figs., 36 refs.

In this paper from the Department of Research, North Carolina Sanatorium System, the authors consider the reasons for variation in the results obtained from B.C.G. vaccination. Investigation showed this to be due to lack of effective standardization, resulting in the production of B.C.G. vaccine with varying protective power. To overcome this they describe a standard system of preparation based on: (1) a colorimetric method for estimating living bacilli in a suspension, which employs the reduction of colourless 2:3:5-triphenyl tetrazolium chloride to red formazan; and (2) estimation of the potency of the vaccine from (*a*) assay of the cord-forming properties of the strain in varying concentrations of "tween 80", and (*b*) the omental index in guinea-pigs, which is obtained 2 weeks after intraperitoneal inoculation and is the ratio between the weight of the affected omentum and the body weight of the guinea-pig.

It was found that these methods taken together gave a consistent assessment of the immunizing power of the vaccine, and that it was possible to produce good or bad results at will by varying the challenge dose and the interval between inoculation and challenge.
John M. Talbot

653. **Antibody Response to Influenza Vaccines Containing the Asian Strain**
J. O. Culver, E. H. Lennette, T. E. Stevens, and R. E. Nitz. *Journal of Immunology* [*J. Immunol.*] **85**, 197–202, Aug., 1960. 1 fig., 12 refs.

The authors, at the Viral and Rickettsial Disease Laboratory, Berkeley, California, investigated the feasibility of making a serological diagnosis of influenzal infection in subjects who had received influenza vaccines. Four groups of about 50 army recruits were studied in terms of antibody response after receiving a placebo, 2 aqueous monovalent A2 vaccines, and an adjuvant polyvalent vaccine with A2, A, A1, swine and B strains of influenza virus respectively.

Ten days after inoculation the mean geometric titre of the complement-fixing antibody to soluble antigen increased from 21 to as high as 58. The titre after inoculation of the adjuvant polyvalent vaccine was similar to that of the better of the 2 monovalent vaccines, but the rise continued beyond the 10th day. No rise in haemagglutinating antibody titre followed inoculation with the aqueous vaccine, but a slight rise was seen against the A1 strain after the adjuvant injection. With the A2 strain of virus, which had been widespread in America over the previous year, the 25 subjects tested fell into 2 groups. Nine who had low pre-inoculation titres showed a trivial rise in haemagglutinating antibody titre; the remaining 16 had a higher initial mean geometric titre of 14, which rose within 10 days to 1,448. The authors stress this evidence that previous exposure to the virus enhances the response to the vaccine and suggest that repeated exposure to the antigens of viruses against which protection was desired might be important. They conclude that a rise in the complement-fixing antibody response occurring more than 10 days after vaccination with an aqueous vaccine could be attributed to influenzal infection. Even after inoculation of an adjuvant vaccine a four-fold increase in titre in a subject with symptoms of influenza would be very suggestive. *G. L. Asherson*

Pharmacology and Therapeutics

654. **Direct Effects of Angiotonin on Peripheral Vessels of Subjects with Normal and Raised Blood Pressures**
J. J. DALY and R. S. DUFF. *Clinical Science* [*Clin. Sci.*] **19**, 457–463, Aug. [received Oct.], 1960. 9 refs.

A comparative study is reported from the Royal and City General Hospitals, Sheffield, of the constrictor effects of a purified preparation of angiotonin (hypertensin I; Skeggs *et al.*, *J. exp. Med.*, 1957, **106**, 439), adrenaline, and noradrenaline. A saline solution of each drug, alternating with 0·9% solution of sodium chloride, was infused into the right brachial artery of 9 normotensive and 6 markedly hypertensive patients at the rate of 3 ml. a minute for 4 minutes, the rate of infusion of adrenaline and noradrenaline being 0·125 μg. of base per minute and that of angiotonin 0·5 Goldblatt unit per minute. Using occlusion plethysmography the authors recorded the changes in the blood flow in the hand produced by adrenaline and noradrenaline before and after infusion of angiotonin. In the normotensive group the infusion of adrenaline caused an average reduction in blood flow of 40% and that of noradrenaline an average reduction of 29%, blood flow returning to normal within 2 minutes of stopping the infusion. A subsequent infusion of angiotonin caused vasoconstriction which persisted for 10 to 20 minutes; repeat infusions of adrenaline and noradrenaline during this period produced further reductions in blood flow averaging 22% and 14% respectively. Whereas the effect of adrenaline and noradrenaline on blood flow was greater in hypertensive than in normotensive patients, that of angiotonin alone was virtually the same in degree and duration in both groups, the mean decrease being 50%. In the hypertensive group the effects of the two adrenergic compounds before and after angiotonin did not differ significantly.

The authors discuss these findings which, they conclude, do not lend support to the view that angiotonin plays a part in the aetiology of chronic hypertension in man. *A. Schott*

655. **Action of Acetazolamide on Respiration. A Study in Healthy and Emphysematous Subjects.** (Action respiratoire de l'acétazolamide: étude chez l'homme à poumons sains ou emphysémateux maintenu sous ventilation constante)
J. J. POCIDALO, F. CORCKET, J. L. AMIEL, J. LISSAC, P. FINETTI, and M. C. BLAYO. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **5**, 582–588, June–July, 1960. 3 figs., 12 refs.

The authors report from the Hôpital Claude-Bernard, Paris, that the intravenous or oral administration of acetazolamide in a dosage in excess of 10 mg. per kg. body weight to normal subjects or to emphysematous patients under standard conditions of respiration resulted in a significant gradient of fall in alveolar carbon dioxide pressure and an increase in partial pressure of CO_2 in arterial blood. They suggest that these results imply that acetazolamide exerts a direct pulmonary effect by inhibiting erythrocyte carbonic anhydrase activity and that its use, in doses sufficient to inhibit this enzyme activity, in patients with chronic respiratory insufficiency or during acute exacerbations of such a state would be of clinical value. *L. A. Elson*

656. **Effect of the Sulphonylureas on Fibrinolysis**
G. R. FEARNLEY, R. CHAKRABARTI, and C. T. VINCENT. *Lancet* [*Lancet*] **2**, 622–625, Sept. 17, 1960. 5 figs., 5 refs.

The effect of sulphonylurea compounds on the fibrinolytic activity of the blood was studied at the Gloucestershire Royal Hospital, Gloucester, 8 patients (7 male and 1 female) suffering from arteriosclerotic disease of the heart or limbs being given tolbutamide or chlorpropamide by mouth. In 7 of the patients there was a decrease in the lysis time of the blood (taken when fasting), indicating an increase in fibrinolytic activity. The authors state that the increase in fibrinolytic activity could not be related to alterations in the blood glucose level. In the remaining patient, who received chlorpropamide, the fibrinolytic activity of the blood decreased.

It is pointed out that a method of enhancing spontaneous fibrinolysis by oral medication has not previously been described. In the authors' view further study is needed to determine the value, if any, of sulphonylurea drugs in arteriosclerotic disease and the nature of their action on the fibrinolytic process. *G. S. Crockett*

657. **Hydroflumethiazide Diuresis in Hospitalized Patients**
G. A. PORTER and N. A. DAVID. *British Medical Journal* [*Brit. med. J.*] **2**, 1044–1048, Oct. 8, 1960. 2 figs., 6 refs.

In this paper from the University of Oregon Medical School, Portland, a trial is reported of the diuretic effect of hydroflumethiazide in 26 patients with severe oedema. The majority of the patients had congestive heart failure but 3 had cirrhosis of the liver and one had nephrosis. They were kept at rest in bed and given a diet providing 1 g. of sodium daily and an unlimited water intake. After a stabilization period of 3 days hydroflumethiazide was given in a dosage of 100 or 150 mg. daily for 3 to 20 days (average 8·1 days).

The clinical response was good or excellent in 16 patients, satisfactory in 4, and fair or poor in 6. Of 23 patients whose weight was determined, 19 showed a loss during treatment, this loss averaging 0·6 kg. a day compared with 0·45 kg. daily during the control period. In most cases there was increased urinary excretion of sodium and chloride and, in 12 cases, increased excretion of potassium. In the majority the serum bicarbon-

ate level rose during administration of the drug and fell again when treatment ceased. A fall in blood pressure was observed in some patients and a rise in the blood urea nitrogen level in others. *Charles Rolland*

658. **Criteria for the Evaluation of Therapeutic Agents in the Treatment of Urinary Tract Infections. I. 6-Demethyl-chlortetracycline**
L. W. DOROSHOW and B. S. ABESHOUSE. *Sinai Hospital Journal* [*Sinai Hosp. J. (Baltimore)*] **9**, 31–36, 1960. 6 refs.

A new antibiotic, 6-demethyl-chlortetracycline, was tried at Sinai Hospital of Baltimore, Maryland, in the treatment of urinary-tract infections in 20 patients who had undergone perurethral prostatic resection and 4 with cystitis and pyelonephritis. A satisfactory result was obtained with a dosage of 600 mg. by mouth daily in all except 7 patients in whom the infection was due to *Aerobacter aerogenes*. From a comparison of these results with those in 58 cases treated with other chemotherapeutic and antibiotic agents the authors gained the impression that 6-demethyl-chlortetracycline compared favourably with these other drugs. [This is a very rough impression.] The correlation between clinical response and bacterial sensitivity *in vitro* was poor.

The criteria for admission to this trial were: (1) an oral temperature of 99° F. (37·2° C.) or higher before operation or when first seen; (2) at least 3 to 5 leucocytes per high-power field in the urine; and (3) urine positive on culture before operation or treatment. Criteria of cure were: (1) no growth on subsequent culture of urine; (2) a tenfold or greater decrease in the estimated viable count of the urine cultures when plated; (3) normal temperature; (4) decrease in or absence of pyuria; and (5) relief of symptoms. *T. B. Begg*

659. **The Effect of Certain Thyroxine Analogues on the Serum Lipids in Human Subjects**
G. S. BOYD and M. F. OLIVER. *Journal of Endocrinology* [*J. Endocr.*] **21**, 33–43, 1960. 13 figs., 24 refs.

Certain analogues of thyroxine have been administered to 26 hypothyroid patients and 132 euthyroid hypercholesterolaemic men with coronary heart disease. The analogues studied were D-thyroxine, 3:5:3′:5′-tetraiodothyroformic acid, 3:5:3′:5′-tetraiodothyronamine, 3:5:3′-triiodo-L-thyronine, 3:5:3′-triiodo-D-thyronine, 3:5:3′-triiodothyroacetic acid, 3:5-diiodo-L-thyronine, 3:5-diiodo-D-thyronine and 3:5-diiodothyroacetic acid.

In both hypothyroid and euthyroid patients, most of these analogues reduced the serum cholesterol without necessarily elevating the basal metabolic rate (B.M.R.). Nevertheless, in euthyroid patients with coronary heart disease several produced angina in the absence of any change in the B.M.R., and this has been regarded as a sign of increased myocardial metabolism insufficient to be reflected in the over-all measure of B.M.R. of all tissues. The possible differential effect of these analogues on the oxygen requirements of various tissues is discussed.

Although it has been possible to maintain low cholesterol levels for periods up to 3 months during the administration of several of these analogues, the dose required for this purpose was often so close to the dose which provoked angina that most cannot be recommended for widespread administration for the reduction of the hypercholesterolaemia frequently found in patients who have coronary heart disease. D-Thyroxine may prove to be an exception and requires further clinical assessment.—[Authors' summary.]

660. **Evaluation of Methohexital for Premedication in Electroshock Therapy**
L. D. EGBERT and S. WOLFE. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 416–419, Sept.–Oct., 1960. 10 refs.

Forty-three patients receiving 276 electroshock treatments were premedicated with "methohexital". In 20 patients a controlled blind study of the recovery period compared methohexital, thiopental, and saline. Induction of hypnosis with methohexital was without incident except for occasional muscular tremors and coughing. Recovery from electroshock therapy was significantly more rapid after methohexital premedication than after thiopental. Therefore, methohexital would appear especially useful in the electroshock therapy of outpatients.—[Authors' summary.]

661. **A Comparison of Morphine and (-)-3-Hydroxy-N-phenacylmorphinan Methanesulfonate (NIH 7525) in Patients with Postoperative Pain**
T. J. DEKORNFELD. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 430–434, Sept.–Oct., 1960. 4 refs.

This is a comparative study of the efficacy of a new analgesic, NIH 7525 ((-)-3-hydroxy-N-phenacylmorphinan methanesulphonate), and morphine in the treatment of postoperative pain. A total of 55 patients who had undergone a variety of operations at Baltimore City Hospitals were divided into three groups, the first group receiving 10 mg. of morphine alternating with 0·5 mg. of NIH 7525 and the second and third groups receiving 10 mg. of morphine alternating respectively with 1 and 2 mg. of NIH 7525. Half the patients were given morphine first and half the experimental drug, double-blind conditions being imposed. The patients were interviewed before and at intervals up to 4 hours after medication. Pain was recorded as being absent or of 4 grades of severity.

It was found that the potency of 0·5 and 1 mg. of NIH 7525 was inferior to that of 10 mg. of morphine, but that the analgesic effect of 2 mg. of NIH 7525 was similar or occasionally superior to that of 10 mg. of morphine.

[These conclusions are drawn from a relatively small number of observations; some of the operations performed are often not followed by pain.]

Mark Swerdlow

662. **Clinical and Experimental Studies on Effects of Succinylcholine.** [Monograph, in English]
Å. WAHLIN. *Acta anaesthesiologica Scandinavica* [*Acta anaesth. scand.*] Suppl. 5, 1–24, 1960. 1 fig., 43 refs.

Chemotherapy

663. **Hormonotherapy of Breast Cancer.** (Гормонотерапия рака молочных желез)
N. D. LAGOVA. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **6**, 3–6, Sept.–Oct., 1960. 30 refs.

Rat carcinoma (of Type RMK–1) was transplanted into adult rats and the effect on its subsequent growth of the following methods of treatment observed: oophorectomy alone, oophorectomy with the addition of adrenalectomy and cortisone, administration of "synoestrol" alone, and a combination of these methods. Tumour growth was retarded by 60% after oophorectomy alone and by 65% when this operation was combined with adrenalectomy and cortisone. However, the administration of synoestrol alone resulted in a retardation of growth of 91%, and when this was combined with oophorectomy, one of 95%; but if synoestrol was given in combination with adrenalectomy and cortisone, the retardation was only 85%. Oophorectomy followed by testosterone accelerated growth of the tumour to 194% of normal. The similarity of the reactivity of this tumour to that of human breast carcinoma permits it to be regarded as an experimental model on which future work on the treatment of breast cancer could be based.

L. Firman-Edwards

ANTIBIOTICS

664. **A New Synthetic Penicillin**
A. H. DOUTHWAITE and J. A. P. TRAFFORD. *British Medical Journal* [*Brit. med. J.*] **2**, 687–690, Sept. 3, 1960. 11 refs.

In this paper and a series of six others [see Abstracts 665–670] it is shown that methicillin ("BRL 1241"), a new synthetic antibiotic, is active against penicillin-resistant staphylococci, has a spectrum similar to that of benzylpenicillin, and is both stable and active in the presence of staphylococcal penicillinase. It is non-toxic, but is unstable in acid medium and therefore cannot be given by mouth.

The authors of the first paper, from Guy's Hospital, London, describe a clinical trial of methicillin on 13 patients, 5 of whom were suffering from pneumonia, 4 from wound infections, and 4 respectively from bronchiectasis, extradural abscess, cerebellar abscess, and urinary infection. The drug was given in a dosage of 1 g. 4-hourly for 5 to 21 days, the patient with intracranial abscess requiring the drug for the longest period. No evidence of *Staphylococcus aureus* infection was detected in any patient after the end of treatment. The injections were as painful as those of benzylpenicillin and prolonged treatment caused local reactions. In one patient, not included in the series, who was sensitive to penicillin there was no reaction to a test dose of methicillin; however, an erythematous rash developed 36 hours after a full dosage of the drug. The blood level of methicillin ranged from 18 to 21 μg. per ml. after 30 minutes and gradually declined to 2 μg. per ml. by the fourth hour. Assay of the urine showed that 75% of the drug was excreted in one day.

Anne Tothill

665. **A New Penicillin (BRL 1241) Active against Penicillin-resistant Staphylococci**
R. KNOX. *British Medical Journal* [*Brit. med. J.*] **2**, 690–693, Sept. 3, 1960. 14 refs.

The second paper in this series describes laboratory investigations carried out at Guy's Hospital Medical School, London, into the antimicrobial and bactericidal activity of methicillin, the effect of penicillinase on this antibiotic, and the action of methicillin on penicillinase formation. Attempts were also made to produce organisms which were resistant to the drug. The serial tube dilution test was used to compare the activity of methicillin, benzylpenicillin, phenoxymethylpenicillin, and "broxil" (phenethicillin) against several common pathogenic organisms. Methicillin was inhibitory to penicillin-resistant staphylococci in a concentration of 2 μg. per ml., but *Salmonella paratyphi* C, which is inhibited by 0·2 μg. of penicillin per ml., was resistant to methicillin. The drug was moderately active against *Neisseria meningitidis* and highly active against the strains of streptococci tested.

Methicillin was equally effective whatever the size of the inoculum, a finding which is in direct contrast to benzylpenicillin, phenoxymethylpenicillin, and phenethicillin. On prolonged incubation (after 7 days) large inocula would grow in high concentrations of methicillin, and this effect is under investigation. Methicillin was not appreciably destroyed by staphylococcal penicillinase. In a concentration of 5 μg. per ml. it had a bactericidal effect on both Oxford and penicillinase-producing (E_3) staphylococci. This was measured by the broth dilution technique followed by viable cell counts at intervals. Under appropriate conditions methicillin was lytic as well as bactericidal to both strains but, as with benzylpenicillin, lysis could be demonstrated only when the cells were in a metabolically active state. The drug was found to induce more penicillinase production in organisms already producing the enzyme, although it was not a substrate. By serial subculture in tubes containing methicillin attempts were made to train penicillin-resistant and penicillin-sensitive staphylococci to become resistant to the drug. This work is still in the preliminary stage, but after three subcultures of E_3 staphylococci in increasing concentrations of the drug the organism was able to grow in a concentration of 18 μg. per ml. and had reverted to the penicillin-sensitive state while no longer producing penicillinase. These findings indicate that the different penicillins have a varying range of antibacterial activity and must be considered separately.

Anne Tothill

666. **Microbiological Studies on Sodium 6-(2:6-Dimethoxybenzamido)penicillanate Monohydrate (BRL 1241) *in vitro* and in Patients**

G. T. STEWART. *British Medical Journal* [*Brit. med. J.*] 2, 694–699, Sept. 3, 1960. 6 figs., 4 refs.

In this third paper the results of sensitivity tests of methicillin against various organisms in liquid and solid media by colony counts of aliquots and by the disk method are reported from Queen Mary's Hospital for Children and the Medical Research Council Laboratories, Carshalton, Surrey. Assays of the antibiotic in body fluids were performed on large-scale assay plates seeded with the test organism, usually *Sarcina lutea*. The unknown fluid was compared in each assay with a range of controls in water, serum, plasma, and albumin, and the results were read from graphs. Urine was heated to minimize contamination and diluted 1:100 with water. The ascending technique was used for chromatography of the drug in urine; after an overnight run the chromatograms were dried and "developed" on assay plates seeded with *S. lutea*.

A preliminary survey of the comparative sensitivities of *Staphylococcus aureus*, three strains of *Streptococcus*, *Pneumococcus*, *Proteus*, coliform bacilli, *Pseudomonas pyocyanea*, *Shigella*, *Salmonella*, *Haemophilus*, and *Clostridium welchii* to benzylpenicillin, phenoxymethylpenicillin, phenoxypropionamidopenicillin, and methicillin was carried out. It was found that 43% of strains of *Staph. aureus* were completely resistant to 10 μg. of benzylpenicillin per ml., whereas all these strains were inhibited by this concentration or less of methicillin, and that 74% were inhibited by phenoxypropionamidopenicillin. The other pyogenic Gram-positive cocci were, in general, more sensitive to the natural penicillins than to the two synthetic ones. Group-A streptococci and pneumococci were uniformly sensitive to the synthetic penicillins and also to benzylpenicillin, but were mostly resistant to methicillin. Gram-negative bacteria, apart from some strains of *Haemophilus*, were highly resistant to methicillin. *Staph. aureus* was sensitive to 1 to 2 μg. of methicillin per ml., which was always bactericidal. At the optimum concentration of 2·5 to 5 μg. per ml. 50% of the cells in the inoculum were killed in one hour and 90 to 95% in two hours. This action was uniform for all the strains tested. All four penicillins had a bactericidal effect on all strains of *Streptococcus* tested. The bactericidal action of methicillin was less rapid than that of benzylpenicillin, but more complete. All strains of *Pneumococcus* were sensitive to all the penicillins. Methicillin in a concentration of 2·5 μg. per ml. inhibited many of the penicillinase-forming strains of *Staphylococcus* even in the presence of a large inoculum. The author states that the drug also acts as a penicillinase inducer and as a substrate and may suffer inactivation after 24 to 48 hours of growth; it could also be completely inactivated by incubation with potent forms of penicillinase derived from *Bacillus licheniformis* and *B. cereus*.

Attempts were made to induce resistance in two strains of *Staph. aureus* and Group-A streptococci by repeated passage through solid and liquid media and *in vivo*. Acquired resistance did not develop and the colonies retained their normal morphological and biochemical properties on subculture on drug-free media. Methicillin did not have a synergic effect with any other penicillin. Individual samples of blood were taken from a number of children at various intervals after injection of a standardized dose of 100 mg. per kg. body weight daily. Inhibitory levels, that is 1 μg. per ml. or higher, were detectable 4 hours after injection, but not longer. Two-thirds of the dose was excreted in the urine unchanged within a few hours of injection, and most of the remainder was excreted in the bile. Hypersensitivity to the drug was shown in an adult volunteer who had previously reacted to benzylpenicillin, the course of both reactions being identical. Methicillin had an unusual activity against staphylococci, but against other organisms it was not as satisfactory as the natural penicillins.

Anne Tothill

667. **Absorption and Excretion of a New Antibiotic (BRL 1241)**

E. T. KNUDSEN and G. N. ROLINSON. *British Medical Journal* [*Brit. med. J.*] 2, 700–703, Sept. 3, 1960. 1 ref.

The fourth paper in this series describes investigations carried out at Beecham Research Laboratories, Brentford, Middlesex, designed to determine a suitable scheme of dosage of methicillin for therapeutic use. The antibiotic was assayed in body fluids, the cup-plate method being used. Before any studies in human beings were undertaken the drug was shown to be non-toxic to animals. In 3 healthy human subjects, a single injection of 100 mg. produced blood levels which were too low to be of therapeutic value, reaching a maximum of only 2·6 μg. per ml. after one hour. In a second experiment 3 healthy subjects received 100 mg. of the drug every 2 hours for 3 doses and one received 200 mg. initially and 100 mg. 2-hourly for two doses. Urine was collected from 2 subjects over a 6-hour period, and the urinary excretion of methicillin was 62% and 61% of the respective total doses. Serum levels were at a maximum (2·2 to 4·1 μg. per ml.) 30 to 60 minutes after injection.

A clinical evaluation of the antibiotic was then carried out on 3 patients with penicillin-resistant staphylococcal infection. The first patient, a man aged 28 with infection of the right hallux after surgical treatment, was given methicillin for 24 hours only, during which time he received a dose every 2 hours to a total of 2·6 g. The maximum blood level of 9·5 μg per ml. was reached 5½ hours after the initial dose; 45% of the dose was excreted in the urine. No staphylococci were isolated from the wound after treatment. The second patient, a girl of 17, was suffering from coagulase-positive staphylococcal pneumonia which had failed to respond to most antibiotics. An initial dose of 450 mg. of methicillin was given intramuscularly, followed 2 hours later by 600 mg. similarly administered. As she was receiving fluids intravenously 750 mg. of the drug was run in over 30 minutes 3-hourly for 2 days; later 1 g. was infused over 15 minutes every 3 hours. The patient subsequently received 1 g. 4-hourly intramuscularly. At 36 hours after the start of treatment the patient was apyrexial and a chest radiograph showed clearing of basal pneumonia. The drug was continued for a further

14 days, a total of 100 g. being given. No toxic side-effects were observed. The serum methicillin level rose to 18 μg. per ml. 3 hours after the start of treatment and before intravenous infusion, a maximum of 46 μg. per ml. being attained. The patient died from coliform septicaemia 14 days after the cessation of treatment; there was then no evidence of staphylococcal infection. The third patient, a man of 58 who was suffering from multiple boils, was given 1 g. of methicillin 4-hourly for 3 days, then 6-hourly for 3 days, after which there was complete resolution of the boils. It is concluded that 1 g. every 4 to 6 hours intramuscularly is a suitable therapeutic dosage for adults. *Anne Tothill*

668. **Report on Clinical Use of BRL 1241 in Children with Staphylococcal and Streptococcal Infections**
G. T. STEWART, H. H. NIXON, and H. M. T. COLES. *British Medical Journal* [*Brit. med. J.*] **2**, 703–706, Sept. 3, 1960. 6 refs.

The authors of this article describe a clinical trial of methicillin in 17 children suffering from staphylococcal infection. The responsible pathogen was isolated in each case and assayed for sensitivity to this antibiotic and other antibiotics. Of the 17 infecting strains, 13 were resistant to benzylpenicillin and 7 belonged to Phage Type 80. One or more antibiotics had previously been given to 12 of the patients. A standard daily dosage of 100 mg. of methicillin per kg. body weight was given intramuscularly for 5 days except to one child with septicaemia who received 150 mg. per kg. per day in 4-hourly doses during 7 days of a 30-day treatment course. Clinical improvement was observed in 14 patients, with complete cure in 7. There were 2 deaths during treatment, both in infants with severe Type-80 infection; one infant, aged 11 days, also had a tentorial tear, and the other, aged 4 months, had fibrocystic disease of the pancreas. Strains of staphylococcus recovered from the patients retained their original sensitivity to methicillin. Streptococci were less sensitive to the drug than to benzylpenicillin, but one child who had bilateral suppurative otitis media and had not responded to penicillin or benzylpenicillin did so to methicillin, with clinical improvement 2 days after beginning treatment. The drug was also given to 11 additional children with sore throat or other streptococcal infections, 10 of whom showed clinical improvement. Pain and tenderness at the site of injection were the only side-effects. During or just after treatment there was replacement of the salivary coccal flora by coliforms in several of the children, and 2 developed superficial infections with *Candida albicans*. *Anne Tothill*

669. **Treatment of Experimental Penicillin-resistant Staphylococcal Lesions with BRL 1241**
R. E. M. THOMPSON, J. L. WHITBY, and J. W. HARDING. *British Medical Journal* [*Brit. med. J.*] **2**, 706–708, Sept. 3, 1960. 3 figs., 7 refs.

At the Bland-Sutton Institute of Pathology, Middlesex Hospital, London, the authors of the sixth paper in this series infected mice with *Staphylococcus pyogenes* isolated from a case of staphylococcal pyaemia. The strain was sensitive to 1·6 unit of benzylpenicillin per ml., 15 μg. of streptomycin per ml., 75 mg. of tetracycline per ml., 3·2 μg. of chloramphenicol per ml., 0·4 μg. of erythromycin per ml., and 1·6 μg. of methicillin per ml. An inoculation of 0·2 ml. of a 1:2 dilution of a broth culture was given into the thigh muscles of each animal; a group of 10 mice was used for each compound tested, with a control group. The diameter of the infected thigh was measured 24 hours after inoculation and then daily for 4 days and finally on the 7th day, the results being expressed as the average daily increase in diameter for the group. The dosage was 50 mg. of methicillin per kg. body weight subcutaneously; 5 doses were given, the first immediately after infection and the others at 24-hour intervals. The infection was completely controlled in all the mice as shown by the absence of an increase in the diameter of the thigh. Similar experiments were carried out with a number of other antibiotics given at the same dose level. Erythromycin was the most effective on a weight-for-weight basis, followed by methicillin, streptomycin, and chloramphenicol; tetracycline and penicillin were relatively inactive. Methicillin was also given in dosages of 1 mg. and 10 mg. daily for 7 days and also in a single dose of 50 mg.; the single dose and 10 mg. daily gave the most protection.
Anne Tothill

670. **Sensitivity of *Staphylococcus pyogenes* to Benzylpenicillin and BRL 1241**
R. E. M. THOMPSON, J. W. HARDING, and R. D. SIMON. *British Medical Journal* [*Brit. med. J.*] **2**, 708–709, Sept. 3, 1960. 1 fig., 6 refs.

The final paper in this series reports a study at the Bland-Sutton Institute of Pathology, Middlesex Hospital, London, of the sensitivity of *Staphylococcus pyogenes* to benzylpenicillin and to methicillin, a total of 118 strains of pathogenic organisms isolated from patients and staff being examined. Qualitative sensitivity tests were carried out on broth–agar slopes on which strips of filter paper impregnated with benzylpenicillin and methicillin were placed. All strains were sensitive to methicillin in a concentration of 1·6 to 3·2 μg. per ml., but only 18% were sensitive to benzylpenicillin.

[Methicillin appears to be an ideal drug for the short-term treatment of staphylococcal infections, but there has not yet been enough experience of the effect of protracted courses of the drug for its value in this respect to be assessed.] *Anne Tothill*

671. **Penicillin V and Phenethicillin Potassium in Serum: Comparison of Concentrations and of Antibacterial Effects**
W. J. MARTIN and D. R. NICHOLS. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **35**, 577–584, Sept. 28, 1960. 11 refs.

At the Mayo Clinic the serum concentrations of phenoxymethylpenicillin and phenethicillin potassium after giving equal doses by mouth were estimated and the antibacterial effect of the serum was studied in 22 subjects. It was found that in 18 of the 22 the concentration of phenethicillin potassium in the serum 2

hours after administration of the last of four 6-hourly doses of 250 mg. was greater than that of phenoxymethylpenicillin after a similar dosage. Mean concentrations titrated by the cup-plate method with *Sarcina lutea* as the test organism were 2·67 μg. per ml. of serum after phenethicillin potassium and 1·65 μg. per ml. after phenoxymethylpenicillin. When the sera were tested against penicillin-sensitive staphylococci little difference was observed between the antibacterial activity of serum containing phenethicillin potassium and that containing phenoxymethylpenicillin. Against strains showing increased resistance to penicillin more sera containing phenethicillin potassium than sera containing phenoxymethylpenicillin were effective in eradicating growth *in vitro*, but frequently only when undiluted.

It is concluded that while phenethicillin potassium does not appear to represent any great advance in clinical therapeutics, it is probably the forerunner of "newer penicillin fractions of possible clinical application that will be produced synthetically". *A. Ackroyd*

672. **Clinical Experience with the New Antibiotic Colistin.** (Klinische Erfahrungen mit dem neuen Antibiotikum Colistin)

H. SCHÖNENBERG. *Deutsche medizinische Wochenschrift Dtsch. med. Wschr.*] **85,** 1714–1717, Sept. 23, 1960.

The author reports his experience with "colistin", an antibiotic of the polymyxin group, in the treatment at the City Paediatric Clinic, Aachen, of children and infants with various infections. The drug is available as the hydrochloride, the sulphate, and the methanesulphonate and the unit of dosage is based on the amount inhibiting the growth of *Escherichia coli* in 1 ml. of nutrient at *p*H 7·2, 1 mg. of the sulphate equalling 18,000 units and 1 mg. of the methanesulphonate 12,500 units. The drug was poorly absorbed when given by mouth, but subcutaneous or intramuscular administration of the hydrochloride in a dosage of 2·5 to 5 mg. per kg. body weight led to blood levels of 25 μg. per ml. after 30 to 60 minutes. Maximum levels were maintained for 6 to 7 hours, followed by a fall to zero within 9 to 12 hours. Urinary excretion was slow, beginning 3 to 4 hours after injection and reaching a maximum in 7 hours (400 μg. per ml. for each 5 mg. per kg. given) and lasting 12 to 15 hours.

Over a period of 6 months 88 infants with gastroenteritis attributed to infection with *E. coli* were treated with a dosage of 100,000 units per kg. by mouth (that is, half a tablet of 250,000 units 4 times daily). (A further 20 infants were treated without bacteriological confirmation of the diagnosis. However, only in 16 cases was the organism typed, 6 showing Type O111 B 4, 5 Type O26 B 5, 4 Type O55 B 5, and one Type O128.) Of these 88 infants, 86 did well as judged by return of the stools to normal and gain in weight. However, 2 showed little response, and 4 premature infants died between 13 and 25 days after the beginning of illness from apnoea and respiratory failure, but no toxic effects could be attributed to the drug. Treatment with colistin was also successful in a small epidemic of Sonne dysentery [number of cases not stated]. One patient had to have a second course before bacterial clearance occurred. In 18 cases of pyuria treated by intramuscular injection the amount given was 500,000 units per kg. body weight in 2 doses per day for 7 days. In 10 cases *E. coli* and enterococci isolated from the urine were cleared by the treatment, but 4 others developed drug resistance. Of 8 cases of pertussis, 3 showed improvement as judged by diminution in the number of coughing spasms. The author is sceptical of the effects of treatment in some of the cases of gastroenteritis and pertussis because of the self-limiting nature of these disorders [an opinion with which the abstracter agrees]. *I. M. Librach*

673. **Resistance Tests and Clinical Trial of Colistin.** (Über Resistenzprüfungen und klinische Erfahrungen mit Colistin)

G. FLEISCHHAUER. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **85**, 1717–1719, Sept. 23, 1960. 28 refs.

At the Paediatric Clinic of the Free University of Berlin comparative resistance tests of "colistin", streptomycin, neomycin, and chloramphenicol were carried out by the agar plate diffusion technique with 5 strains of urinary coliform bacilli, 8 of *Salmonella*, and 109 enteropathic strains of *Escherichia coli*, including all the most common types. The results were read after 24 hours' incubation. Of the strains of *E. coli* tested, 64 were inhibited satisfactorily by streptomycin, but only 29 by chloramphenicol. Neomycin and colistin were uniformly successful, except that the latter failed to inhibit *E. coli* Type O26 B 6. Salmonellae and urinary coliforms gave similar results, except that two strains of *Salmonella* were resistant to chloramphenicol.

During May and June, 1960, 35 infants with enteritis were treated with colistin. In 20 cases the stool culture was negative, but the remaining 15 gave positive results, enabling the infecting organism to be identified. In 26 cases the stools became normal in 24 hours. The looseness of the stools which usually follows administration of chloramphenicol was not observed after colistin. The drug suppressed all Gram-negative organisms in the intestine, these being replaced by a Gram-positive flora. In the one case of salmonellosis treatment with neomycin led to clinical improvement, but bacterial clearance was subsequently achieved only by giving a 5-day course of colistin. The dosage of the latter in all cases was 100,000 to 150,000 units per kg. body weight, that is, 5 to 7·5 mg. of the sulphate, a course of treatment consisting of 4 doses daily for 5 days of tablets of colistin sulphate each containing 250,000 units (12·5 mg.). The author appears to be enthusiastic about the effects, both therapeutic and prophylactic, of colistin in infants with gastrointestinal symptoms [an enthusiasm which the abstracter does not entirely share]. *I. M. Librach*

674. **The Absorption and Excretion of N-(pyrrolidinomethyl) Tetracycline**

G. A. CRONK, F. H. BUCKWALTER, W. B. WHEATLEY, and H. ALBRIGHT. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **241**, 1–13, Jan., 1961. 8 figs., 4 refs.

Infectious Diseases

675. **Comparison of Dithiazanine Iodide and Pyrvinium Pamoate in the Treatment of Enterobiasis (Pinworms)**
A. I. SANDERS and W. H. HALL. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **56**, 413–416, Sept., 1960. 9 refs.

Dithiazanine iodide was given in multiple doses to 25 patients with enterobiasis (pinworms). Treatment was discontinued in 14 because of vomiting or diarrhea. Treatment was completed in 8 of the 12 children who received enteric coated tablets and in only 2 of 11 children who were given uncoated tablets. Pinworm ova were not found in any of the patients who completed the treatment, either in full or half doses. A single dose of pyrvinium pamoate was administered to 25 children and 4 adults with pinworms. There were no side effects except in one child who vomited once 2 hours after administration of the drug. The treatment eliminated pinworms in all but this one patient. The treatment is simple, safe, and effective. It is especially recommended for treatment of groups in institutions and families.—[Authors' summary.]

676. **Acute Infectious Arthritis in the Aged and Chronically Ill**
R. F. WILLKENS, L. A. HEALEY, and J. L. DECKER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **106**, 354–364, Sept., 1960. 1 fig., 21 refs.

This is an account of 19 cases of acute septic arthritis in aged or chronically ill patients seen during a 5-year period at the King County and Seattle Veterans Administration Hospital, Washington. In 15 cases the diagnosis was based on the culture of organisms from the synovial fluid, in one case organisms were identified in a smear of the joint fluid, and in 3 cases the presentation and clinical course were characteristic. The patients' ages ranged from 45 to 77 years. In 16 cases the arthritis was monarticular and in 3 polyarticular. The knee-joint was most commonly involved, then the shoulder, interphalangeal joints, ankle, and elbow, in that order. In 9 cases the infecting organism was *Staphylococcus aureus*, which in some cases was resistant to the usual antibiotics, and in at least 3 of these there was reason to believe the infection had been acquired in hospital. The next commonest organism was the pneumococcus. In 12 cases the infection appeared to be blood-borne from infection elsewhere (pneumonia, empyema, superficial infection, osteomyelitis). In 6 the infection entered the joint by penetrating trauma, received in 3 cases during intra-articular therapy. Four patients had chronic rheumatoid arthritis and 8 were chronic alcoholics.

In 11 cases conservative therapy with antibiotics was used and the results appeared to be as good as in cases treated by open drainage in addition to antibiotics. If adequate antibiotic therapy was instituted promptly the results were good. The diagnosis was difficult in some cases owing to failure to realize that an increase in joint symptoms was not due to an exacerbation of pre-existing arthritis or disease. The importance of paracentesis of the joint whenever there is doubt is stressed. The "leukocrits" of joint fluid from successive paracenteses were valuable for following progress. Vancomycin proved helpful in some of the cases due to resistant staphylococci. *C. Bruce Perry*

VIRAL DISEASES

677. **The Influence of Salk's Vaccine on the Course of Acute Anterior Poliomyelitis.** [In English]
F. QUAADE. *Acta medica Scandinavica* [*Acta med. scand.*] **167**, 427–430, 1960. 6 refs.

Intracutaneous Salk-vaccination as employed in Denmark since 1955 seems to have somewhat modified the course of acute anterior poliomyelitis. This is most evident in a reduction of time in hospital and spinal fluid disturbances, and a prolongation of the prodromal stage. The effect of the vaccination seems to appear also as a milder clinical course of the disease regarding the number and extension of the paralyses. At the same time the investigation confirms the experience that severe poliomyelitis may occur in fully vaccinated persons.—[Author's summary.]

678. **Persistence of Immunity after Administration of Formalin-treated Poliovirus Vaccine**
J. E. SALK. *Lancet* [*Lancet*] **2**, 715–723, Oct. 1, 1960. 16 figs. 18 refs.

The author reports studies on immunization against paralytic poliomyelitis based on the paralysis rate experienced in the U.S.A. in 1959 and endeavours to establish the parameters within which protection against poliomyelitis paralysis could be induced with a high degree of certainty. During that year 5,267 cases of poliomyelitis with residual paralysis, mostly due to the Type-1 virus, were recorded. There was an inverse linear relationship between the paralysis rate (plotted on a logarithmic scale) and the number of doses of formalin-treated trivalent poliovirus vaccine administered at unspecified times. This applied reasonably well to all age groups. Even a single dose of vaccine conferred some immunity, and "the linear relationship indicated that each successive dose reduced the remainder of the susceptibles by the same proportion as did the first dose".

If this represents the general rule for vaccines, hypothetical curves describing the cumulative percentage conversions indicate that in 1959 the average effect for a single dose of vaccine was just over 50% and for 4 doses 96%. With vaccines of low potency multiple

doses become less and less efficient for immunization, and conversely, the greatest efficiency is associated with vaccines that approximate a full effect after one dose. This suggests that immunity results from the first effective antigenic stimulus and that if a critical level of response can be achieved after one injection uniform immunization by one dose of a killed virus vaccine is theoretically possible. The diminishing return with successive doses emphasizes the desirability of achieving the highest level of immunization with the fewest injections, and relationships suggest that the use of vaccines of greater conversion efficiency would considerably reduce vaccine failures.

It has been observed that the antigenic mass initially given affects not only the level of antibody developed initially, but also the persistence of demonstrable antibody. Dosage–response curves obtained from data following the use of various amounts of reference vaccine "A" indicate that there is a critical antigenic content below which the percentage of persons with antibody titres of 1:4 or more one year after vaccination falls sharply; the approximate relative amounts of the respective antigens which would be needed to achieve this level of potency can be deduced. It would seem that an antigen content increased 8-fold to 10-fold over the average of the recent past is in the range of the minimum required for optimum effectiveness for Type-1 virus. Responses to Type 2 suggest that there is a difference in degree and persistence of immunological response to different strains of virus.

It was ascertained that the level of demonstrable antibody a year after a booster dose is a guide to the level during the next 6 years at least, and for predicting the decline in antibody level with time a line connecting the levels one and 2 years after the booster is the most informative.

These studies suggest that lasting protection against poliomyelitis should be attainable with a single dose of formalin-treated virus vaccine and that the spread of virus in the population could be totally suppressed.

A. Ackroyd

679. **An Outbreak of Acute Laryngotracheobronchitis Associated with Para-influenza-2 Virus**

M. S. Pereira and O. D. Fisher. *Lancet* [*Lancet*] **2**, 790–791, Oct. 8, 1960. 8 refs.

During an outbreak of laryngotracheobronchitis in the winter of 1958–9 13 children aged from 4 months to 4 years were admitted to the Medway and Gravesend group of hospitals. The symptoms were those of upper respiratory tract infection accompanied by a croupy cough, hoarse voice, and inspiratory stridor which was often associated with respiratory distress and cyanosis. In severe cases there were adventitious sounds in the lungs. Treatment consisted in putting the patient in a steam tent and administering chloramphenicol, but one boy aged 11 months died. Clinical details are given of this case, and of 3 others in which laboratory investigations yielded evidence of infection with para-influenza-2 virus (the croup-associated (C.A.) virus). Further particulars are also given of the treatment of these and the other cases, and the results of pathological investigations are reported.

In the virus studies (carried out at the Virus Reference Laboratory, Colindale) throat swabs from 5 of the children were inoculated into cultures of HeLa cells, monkey kidney tissue, and human amnion. After 5 days' incubation at 37° C. two of these swabs yielded virus strains, which were detected by the haemadsorption technique in monkey kidney cultures and later identified by neutralization with specific rabbit antiserum as para-influenza-2 virus. The characteristic effect of the virus on monkey kidney tissue cultures and also on those of human amnion in the form of syncytial masses with large holes in the cell sheets did not appear until after incubation for a further 4 to 8 days. In additional studies with para-influenza-2 virus as antigen, complement-fixation tests were performed on paired sera from 2 patients, from one of whom the virus had been previously isolated. In each case a greater than 4-fold rise in titre was found between specimens taken early in the illness (2 to 4 days) and those taken at a later date (11 to 12 days).

In view of the fact that a further strain of para-influenza-2 virus was isolated by the authors from a child with respiratory infection in Cardiff, the suggestive evidence of such infection obtained by antibody surveys in Sheffield, and the isolation of 5 strains of virus by Gardner *et al.* (*Brit. med. J.*, 1960, **1**, 1077; *Abstr. Wld Med.*, 1960, **28**, 412) in the north of England, together with their own findings, the authors suggest that the incidence of para-influenza-2 virus in acute laryngotracheobronchitis in Great Britain merits further investigation.

Joyce Wright

680. **Virus Influenza and the Involvement of the Cardiovascular System.** (Поражение сердечно-сосудистой системы при вирусном гриппе)

V. N. Djačenko and M. I. Lizunova. *Советская Медицина* [*Sovetsk. Med.*] **24**, 56–60, Sept., 1960. 2 figs., 3 refs.

Of 674 patients admitted to hospital during 1958 and 1959 suffering from cardiovascular disease, all attributed the appearance of oedema, dyspnoea, or precordial pain to a recent attack of influenza. This disease affected the myocardium mainly in patients with atherosclerosis or coronary sclerosis, giving rise to attacks of angina or to circulatory failure of Grade IIA or IIB. Post-influenzal myocarditis was the most serious complication in young adults aged 22 to 31 years with no previous history of cardiac disease. The signs consisted in a dull retrosternal ache, subnormal temperature, palpitation, enlargement of the heart, tachycardia of 110 to 120 per minute, an increased haemoglobin concentration (up to 114%), an increased erythrocyte count (up to 5,600,000 per c.mm.), and a slight leucocytosis. The erythrocyte sedimentation rate was not raised and the blood pressure was normal. Nearly all these patients were admitted in the 3rd week of the disease. The electrocardiogram showed the P–R interval to be increased to 0·2 second and the QRS to 0·1 second. The cardiovascular complications of influenza are thought to result from toxic myocarditis and from changes in the blood coagulation mechanism, the latter factor being more important in older, atherosclerotic subjects. *S. W. Waydenfeld*

681. **The Effects of Antibiotics on the Clinical Course and Complications of Measles.** (Влияние антибиотиков на течение кори и ее осложнений)
M. A. DADAŠ'JAN and V. A. VOLYNSKAJA. *Советская Медицина* [*Sovetsk. Med.*] **24**, 64–69, Sept., 1960. 14 refs.

Of 288 children with measles (68 under 1 year of age, 128 aged 1 to 2 years, 52 aged 2 to 5 years, and 40 over 5 years) who were treated with antibiotics, 77 received these drugs in the incubation period, 82 in the prodromal stage, and 129 on the 1st or 2nd day after appearance of the rash. A group of 82 children aged over 2 served as controls. It was found that the course of the disease was not influenced in any direction by sulphonamides, penicillin, or streptomycin when these were given in the early stages of the disease, the incidence of complications in the various treatment groups being closely comparable. The lack of effect of antibiotics in early measles pneumonia confirmed the previously accepted view concerning the viral nature of this condition. Only wide-spectrum antibiotics such as "levomycetin" and the tetracyclines, given early, exerted a slightly favourable effect on the course of measles in the form of lower temperature and less toxaemia, but complications still occurred in younger patients. However, the administration of antibiotics combined with other measures produced good results in the treatment of complications, whether or not these were pulmonary, or septic or necrotic. Side-effects of antibiotic therapy were observed in 34 children, mainly those (28) under 2 years of age, and included thrush (20 cases), peri-anal irritation (5), skin rashes (4), and leucopenia and agranulocytosis (15). Antibiotic-resistant organisms were isolated from 18 of 102 children. It is concluded that great care must therefore be exercised in selecting cases of measles likely to benefit from a course of antibiotics.

S. W. Waydenfeld

BACTERIAL DISEASES

682. **Brucellosis of the Bones and Joints: Experience with Thirty-six Patients**
P. J. KELLY, W. J. MARTIN, A. SCHIRGER, and L. A. WEED. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **174**, 347–353, Sept. 24, 1960. 3 figs., 16 refs.

A study is reported from the Mayo Clinic of 36 patients with brucellosis of the bones and joints, most of whom were farmers or meat handlers, some giving a history of drinking raw milk from an infected herd. In some cases the signs and symptoms included pyrexia, loss of weight, and localized pain and tenderness. The findings were not always typical of an infective process; anaemia, leucocytosis, and a high erythrocyte sedimentation rate were present in a few cases only. Localized chronic hydrops was regarded as a significant feature of brucellosis of the prepatellar bursa. In brucellosis of the bone the radiological appearances were not those of a specific form of osteomyelitis. One case of bacteriaemia was detected, but for the most part the diagnosis could be established with certainty only by culture of organisms of the *Brucella* group from specimens of tissues; the strains most commonly isolated from skeletal lesions were *Brucella suis* and *B. abortus*. Agglutination tests were of diagnostic value when the serum contained brucellar agglutinins in high or increasing titre. It was noteworthy, however, that the titres were often low in 22 patients with culturally proved skeletal disease. Skin testing techniques were not considered to be reliable.

As regards treatment, surgery was seldom required in cases of spondylitis. Wide drainage was used for osteomyelitis, special care being taken to avoid secondary pyogenic infection. Good results were obtained from oral administration of 500 to 750 mg. of tetracycline every 6 hours and intramuscular injection of 0·5 g. of streptomycin twice daily for 4 weeks. Audiometry and vestibular tests were carried out as precautionary measures for detecting early signs of complications due to streptomycin therapy. *A. Garland*

683. **The Prevention of Type Specific Immunity to Streptococcal Infections Due to the Therapeutic Use of Penicillin: Occurrence of Second Attacks Due to the Same Type of Group A Hemolytic Streptococci.**
B. B. BREESE, F. A. DISNEY, and W. B. TALPEY. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **100**, 353–359, Sept., 1960. 18 refs.

Several workers, notably McCarty, have drawn attention to the danger that the over-enthusiastic treatment of streptococcal infections with penicillin in childhood may interfere with the later development of that type-specific immunity which is considered to be the foundation of adult immunity to such infections. In this paper from the University of Rochester School of Medicine, New York, the authors present data on 6,198 streptococcal infections occurring over an 11-year period in 3,047 children in private practice which were adequately treated with various types of penicillin. Approximately 75% of these patients had had more than one attack. It was possible to group and/or type some two-thirds of the infecting streptococci, and of these, 51·7% were of Group A and of specific type, 43·5% were of Group A but non-typable, and only 4·8% were of groups other than A. Of the 473 children with two or more Group-A infections of known type (omitting 345 who were infected with non-typable strains more than once), 286 were attacked by two different specific types and 187 by the same type of Group-A streptococcus. Of these 187 second attacks, 138 were considered to be true clinical recurrences, the interval between the first and second attacks ranging from 8 days to 5 years. The remaining 49 children were regarded as carriers.

The authors point out that although these data seem to suggest that type-specific immunity was not developing in the children with repeated streptococcal infections treated with penicillin, epidemiological evidence based on the age distribution of all the cases over the period indicates that such immunity to streptococcal infections was in fact developing in this child population and therefore, the authors conclude, "fears that the use of penicillin may lead to the development of a non-immune adult population seem ungrounded". *A. Ackroyd*

Tuberculosis

DIAGNOSIS AND PROPHYLAXIS

684. **Multiple-puncture Vaccination in the Newborn with Freeze-dried B.C.G. Vaccine**
M. I. GRIFFITHS. *British Medical Journal* [*Brit. med. J.*] **2**, 1116–1119, Oct. 15, 1960. 1 fig., 12 refs.

A total of 2,221 newborn infants have been inoculated with British freeze-dried B.C.G. vaccine by multiple-puncture vaccination between March, 1959, and April, 1960. Details of technique are described and significant factors discussed. The results of multiple-puncture vaccination are compared with those of intradermal vaccination.

It is suggested that, using the British freeze-dried vaccine, optimal results are obtained by firing 20 needles to a depth of 2 mm. through a vaccine concentration of 83 mg. per ml. It is hoped that by further improvement in technique the efficiency of multiple-puncture vaccination may be raised to the standard produced by intradermal vaccination.—[Author's summary.]

685. **Freeze-dried B.C.G. Vaccine. Stability of the Vaccine under Different Conditions of Storage and Persistence of Tuberculin Sensitivity in Schoolchildren after Vaccination**
SECOND REPORT TO THE MEDICAL RESEARCH COUNCIL BY THEIR COMMITTEE ON THE STANDARDIZATION OF FREEZE-DRIED B.C.G. VACCINE. *British Medical Journal* [*Brit. med. J.*] **2**, 979–986, Oct. 1, 1960. 4 figs., 7 refs.

A previous report from this committee of the Medical Research Council on the standardization of freeze-dried B.C.G. vaccine (*Brit. med. J.*, 1958, **1**, 79; *Abstr. Wld Med.*, 1958, **24**, 173) demonstrated that the ranges of variation of viable count in the British freeze-dried B.C.G. vaccine and the Danish liquid vaccine were similar and that the conversion rates produced by the dried vaccine were satisfactory. In this further study the stability of the vaccine after storage for various periods and at different temperatures and also the persistence of tuberculin sensitivity after vaccination have now been investigated.

Viable counts in both the dried and liquid vaccines were performed as previously described in the earlier report cited above, while similar counts on the liquid vaccine were also carried out at the State Serum Institute, Copenhagen, and correlated well with those determined at the M.R.C. Biological Standards Control Laboratory, London, the mean counts being $18{\cdot}9 \times 10^6$ per ml. and $19{\cdot}2 \times 10^6$ per ml. respectively. The stability of batches of the freeze-dried vaccine stored at 4° C., at room temperature (average 23° C.), at 37° C., and at 45° C. was examined over periods of 45 to 70 weeks. Of 5 batches stored at 4° C., 4 maintained approximately the same viable count over periods of 45 to 65 weeks, while the 5th batch showed some fall over a storage period of 70 weeks. At room temperature, however, there was a considerable fall in the viable count over periods of 30 to 60 weeks, while at 37° C. the fall was more rapid; both at this temperature and at 45° C. there was a very rapid fall in the first few days of storage.

Mantoux testing of children inoculated with the liquid vaccine, freeze-dried vaccine stored at 4° C., or freeze-dried vaccine stored at room temperature was performed. Examination of the results obtained at one to 4 months and again at 10 to 13 months after vaccination showed that, with the exception of one batch, the conversion rates obtained with the freeze-dried vaccine were only slightly lower than those obtained with the liquid vaccine; the possible reasons for the anomalous results obtained with the one batch of dried vaccine are fully discussed. A separate test was made to determine whether the second post-vaccination tuberculin test was influenced by the first one, but no evidence was found that this was the case. It is concluded that the British freeze-dried vaccine is a satisfactory agent for prophylaxis against tuberculosis, but that care must be taken, for example during its transit, not to allow it to remain at a temperature above 20° C. for longer than one week.

John M. Talbot

686. **Detection of Pulmonary Tuberculosis by Sputum Survey**
L. ERIN. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 363–366, Oct., 1960. 8 refs.

The efficiency of sputum surveys in the detection of cases of tuberculosis has been studied in a mining town in Glamorgan. To this end 2,001 specimens of sputum were collected, of which 1,982 were successfully cultured. As a result 4 specimens were found to contain tubercle bacilli. Subsequent chest radiography confirmed the presence of pulmonary tuberculous lesions in the cases concerned. A comparison of the financial cost of the sputum survey with that of two mass radiography surveys showed the former to be much less expensive in terms of the number of sputum-positive cases discovered. The findings of the survey indicated an effective way of discovering cases of tuberculosis which might be used with advantage in certain circumstances. A disadvantage of sputum surveys is their failure to detect other than sputum-positive tuberculosis.

T. M. Pollock

687. **Prophylactic Isoniazid in Nurses in a Tuberculosis Hospital**
B. A. DORMER and M. M. WOOD. *Lancet* [*Lancet*] **2**, 837–840, Oct. 15, 1960. 5 figs., 4 refs.

The authors describe the prophylactic treatment with isoniazid of nurses at King George V Hospital, Durban, which has 1,300 beds for non-European tuberculous patients, two-thirds of whom are admitted with far-advanced disease. Beginning in September, 1955, 300 mg. of isoniazid was given daily in a single dose to all non-European nursing aides, numbering 600, of whom

16% were tuberculin-negative on appointment to the hospital. After 4 years of this scheme 68% of the nurses were thought to be taking the drug regularly. Of the 600 nurses, 4 developed tuberculosis—one in 1958 and 3 in 1959—compared with 51 of a similar group of nurses during the period 1946–55.

Tubercle bacilli recovered from 3 of the nurses who developed tuberculosis in spite of isoniazid prophylaxis showed varying degrees of isoniazid resistance, but all 3 patients responded satisfactorily to treatment with the drug or its derivatives and streptomycin, with or without PAS. The outcome, judged by the speed of sputum conversion, radiological appearances, and duration of absence from duty, compared favourably with that in patients in whom tuberculosis developed without previous isoniazid prophylaxis. It is concluded that isoniazid prophylaxis is worth while in groups of people exposed to heavy tuberculous infection.

Discussing B.C.G. prophylaxis, the authors state that this could help only the relatively few who were tuberculin-negative on appointment. In all, 83 nurses received B.C.G. vaccination before the end of 1955 and of these, 3 developed tuberculosis, an incidence far greater than in the larger group given isoniazid prophylaxis. It is of interest that over 80% of the nurses who were tuberculin-negative on appointment and did not receive B.C.G. vaccination became tuberculin-positive within a year. Nevertheless, of 12 nurses initially tuberculin-negative who developed tuberculosis, only 3 did so soon after conversion, the remaining 9 up to 5 years later.

A. J. Karlish

RESPIRATORY TUBERCULOSIS

688. **The Estimation of Maximal Breathing Capacity by Means of Chest Fluoroscopy and Inspiratory Roentgenograms: a Study in Patients with Pulmonary Tuberculosis**

G. L. SNIDER and A. R. SHAW. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **82**, 314–321, Sept., 1960. 3 figs., 20 refs.

A study was undertaken at the Municipal Tuberculosis Sanitorium and Michael Reese Hospital, Chicago, " to compare the accuracy of estimation of maximal breathing capacity from chest fluoroscopy with an estimate made from frontal chest roentgenograms ". Two groups each containing 100 patients with pulmonary tuberculosis whose maximal breathing capacity had been assessed by both methods and also directly were selected and the results analysed. This showed a mean error for fluoroscopic examination of 11·5% (range −39% to +39%); the mean error for radiographic examination was 17·1% (range −54% to +35%). Taking the two groups separately, the mean error on fluoroscopic examination in the first 100 cases was 13·1%, while that for the second 100 cases was 9·6%. As the second group was investigated two years after the first it is suggested that this reflects the development of the fluoroscopist's skill.

Fluoroscopy is recommended as being more accurate than radiographic estimation of ventilatory function, and also as being cheaper and more readily available. The authors conclude, however, that ventilatory function tests are still necessary when more exact details are required.

Franz Heimann

689. **Tuberculosis Disseminators: a Study of the Variability of Aerial Infectivity of Tuberculous Patients**

L. SULTAN, W. NYKA, C. MILLS, F. O'GRADY, W. WELLS, and R. L. RILEY. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **82**, 358–369, Sept., 1960. 2 figs., 19 refs.

As part of a quantitative study of air-borne infection at the Veterans Administration Hospital, Baltimore, the authors have determined the frequency of occurrence of tuberculous infection in guinea-pigs exposed to air exhausted from a 6-bed tuberculosis ward. During the 2 years of study 77 patients who had extensive cavitary tuberculosis of the lung and whose sputum contained large numbers of acid-fast bacilli had occupied the ward. Six-week-old guinea-pigs were quarantined for 3 to 4 weeks and then tuberculin-tested by intradermal injection. Reactions were read at 24 and 48 hours, and animals giving negative reactions were admitted to the test chamber.

Altogether 71 guinea-pigs became infected with tuberculosis. The infecting organism was cultured and drug-resistance studies were carried out on 48 of these animals, and it was found that 35 of the infections had been caused by only 3 patients. It is suggested that this high rate of infectivity is related to the production by these patients of large numbers of bacilli " unusually capable of withstanding the rigors of air-borne transmission ".

Franz Heimann

690. **Is Cavity Closure in Pulmonary Tuberculosis Influenced by Bed-rest?**

N. WYNN-WILLIAMS and J. B. SHAW. *Tubercle* [*Tubercle (Lond.)*] **41**, 352–357, Oct., 1960. 5 refs.

This paper describes an attempt to estimate the effect of rest in bed and physical activity on the fate of cavitation in pulmonary tuberculosis. During the period July, 1957, to March, 1959, 70 patients admitted to Bedford General Hospital and St. Mary's Hospital, Luton, with proved cavitation, positive sputum, and organisms sensitive to streptomycin, *p*-aminosalicylate (PAS), and isoniazid, were allocated at random equally to two treatment groups. Patients in the " rest " group remained in bed except for toilet purposes. They were allowed to get up only if the cavity closed before 6 months; if it remained open after this time reassessment was made as regards further treatment, which might be surgery, longer rest, or increased activity. Patients allocated to the " exercise " regimen remained in bed only if they felt ill or were febrile. They were allowed to do what they liked short of taking exercise that led to breathlessness or fatigue. Nearly all patients received 1 g. streptomycin, 12 g. PAS, and 200 mg. isoniazid, all daily, for the first 3 months, followed by 1 to 2 years' treatment with PAS and isoniazid.

The trial was completed by 62 patients. After 6 months' treatment there was no difference between the

two groups in the rate of cavity closure, sputum conversion, or reduction in erythrocyte sedimentation rate. Similar results were found after one year. Patients in the " rest " group were off work more than twice as long as those in the " exercise " group. *B. Golberg*

691. **Intrapleural Hydrocortisone in Tuberculous Pleural Effusion**
K. S. MATHUR, R. PRASAD, and J. S. MATHUR. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 358–362, Oct., 1960. 10 refs.

The effect of intrapleural injection of hydrocortisone in addition to the usual chemotherapy in the treatment of tuberculous pleural effusion was studied in 50 patients admitted to Sarojini Naidu Hospital, Agra, India. The patients were divided into 2 equal groups, both receiving the same chemotherapy with streptomycin and isoniazid [dosages not stated]. In one group, which served as a control, fluid was aspirated only for the relief of symptoms. Pleural biopsy was performed on the other group and at the same time hydrocortisone was injected intrapleurally (250 mg. in the first 10 cases and 125 mg. in the remaining 15). Therapeutic aspiration was not done. In cases in which fluid persisted a second or third biopsy of parietal pleura was carried out and the same dose of hydrocortisone was repeated fortnightly up to a maximum of 4 instillations. The majority of patients (18) received only one instillation. Patients were followed up for 6 to 12 months after discharge from hospital.

A rapid fall in temperature (reaching normal in 24 hours in 21 cases) and reduction in erythrocyte sedimentation rate with improvement in general condition were noted in most of the hydrocortisone-treated group. Fluid was absorbed within 15 days in 18, within 30 days in 3, and within 60 days in 2 cases in this group. In comparison, in the control group fluid cleared within 30 days in 2 and within 60 days in 7; in no case did fluid clear within 15 days, and in 16 cases it persisted for more than 60 days. Among the hydrocortisone-treated patients 16 showed no residual pleural thickening and 7 only slight thickening, whereas varying grades of thickening remained in most of the controls. *B. Golberg*

692. **Accidents Due to Isoniazid in the Course of Prolonged Treatment of Tuberculosis in Children.** (Accidents provoqués par l'isoniazide au cours des traitements prolongés de la tuberculose de l'enfant)
J. CHAPTAL, R. JEAN, A. CRASTES DE PAULET, H. BONNET, M. PETIT, and R. GUILLAUMOT. *Pédiatrie* [*Pédiatrie*] **15**, 623–634, 1960. 25 refs.

From the Clinique des Maladies des Enfants, Montpellier, the authors report 4 cases of acute encephalopathy which occurred during the treatment with isoniazid of tuberculous children aged 4, 8, 9, and 9 years respectively, of whom 3 had meningitis. The dose of isoniazid was high—30 mg. per kg. body weight daily. The signs and symptoms included convulsions in 3 cases, gross psychological disturbance in 2, and severe vertigo in one. The symptoms did not appear until after several weeks of treatment; all the children recovered without sequelae, even though the treatment with isoniazid was continued. It is considered that a deficiency of vitamin B_6 (pyridoxine) is the cause of such symptoms and was shown to be so in the present cases. [It is advisable to give pyridoxine prophylactically to all children receiving isoniazid.] It was shown that steroids apparently have some protective value against the neurological complications in these cases, although the mechanism of their action is not known. *John Lorber*

693. **Prednisolone in the Treatment of Acute Extensive Pulmonary Tuberculosis in West Africans**
W. J. BELL, P. P. BROWN, and D. W. HORN. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 341–351, Oct., 1960. 18 refs.

The Tuberculosis Research Unit of the West African Council for Medical Research, Accra, Ghana, has carried out a controlled trial to determine whether the addition of prednisolone to the standard chemotherapy hastens clinical and radiographic improvement and clears the sputum more rapidly of tubercle bacilli in acute extensive pulmonary tuberculosis. The investigation was confined to 100 West African males aged between 16 and 40 whose disease had been previously untreated and whose sputum contained tubercle bacilli sensitive to the drugs employed. All 100 patients were given streptomycin sulphate, 1 g. daily, sodium *p*-aminosalicylate 4 g. thrice daily, and isoniazid, 100 mg. thrice daily, for 12 weeks. Prednisolone, 5 mg. four times daily, was given in addition to 49 of the patients allocated at random, the remaining 51 patients acting as controls. The prednisolone treatment was started after one week's chemotherapy, continued for 8 weeks, then tailed off for 2 weeks; none was given in the final week.

During the first month of treatment there was a statistically significant acceleration of improvement in general condition in severely ill patients or those in poor condition in the group receiving additional prednisolone as compared with the controls. No significant differences were found, however, in weight change, radiological improvement, or cavity closure. Clearance of tubercle bacilli from the sputum on the other hand was not hastened, there being an initial rise in the bacterial count in the prednisolone-treated group. Finally, a well-marked increase in the number of circulating leucocytes, including eosinophils, was noted in this group. *B. Golberg*

694. **Ethionamide (' 1314 ') with Streptomycin in Acute Tuberculosis of Recent Origin in Uganda Africans: a Pilot Study**
P. W. HUTTON and I. M. TONKIN. *Tubercle* [*Tubercle* (*Lond.*)] **41**, 253–256, Aug., 1960. 7 refs.

Ethionamide was given with streptomycin to 7 patients with acute rapidly progressive tuberculosis in Uganda Africans, previously untreated. Clinical, bacteriological and radiographic improvement was observed in all cases. One patient produced a single colony culture resistant to streptomycin, isoniazid, ethionamide and PAS after 6 months. All previous cultures were sensitive. This was the only positive culture obtained in the 6 patients in whom cultures were done at 6 months.

This pilot study suggests that further investigation of this drug combination is desirable.—[Authors' summary.]

Venereal Diseases

695. **Clinical Evaluation of Metronidazole: a New Systemic Trichomonacide**
L. WATT and R. F. JENNISON. *British Medical Journal* [*Brit. med. J.*] **2**, 902–905, Sept. 24, 1960. 12 refs.

It is believed that local treatment of vaginitis due to *Trichomonas vaginalis* often fails because extravaginal foci remain untouched. Durel *et al.* (*Brit. J. vener. Dis.*, 1960, **36**, 21) have reported successful results in both men and women with a new imidazole derivative, metronidazole (1-β-hydroxyethyl-2-methyl-5-nitroimidazole). In the present paper the results obtained with metronidazole in 50 female patients treated at St. Mary's Hospital for Women, Manchester, for vaginitis due to *T. vaginalis* are described. The drug was given by mouth in a dosage of 600 mg. daily for one week. Relief from irritation was rapid and there was a dramatic clinical improvement within a week in cases of recent onset. Chronic infections improved more slowly, but 44 of the patients showed no clinical or laboratory evidence of infection at the end of treatment. Side-effects, which were not usually severe, occurred in 11 patients, but it was necessary to discontinue treatment only in one patient who vomited when receiving 1,200 mg. daily. This high dosage was given to the 6 patients who did not respond initially, and 3 of them appeared to benefit. It is considered that the failure of treatment in the remaining 3 was not due to re-infection, but to poor absorption of the drug or to the greater resistance of the organism. *Janice Taverne*

696. **Systemic Treatment of *Trichomonas vaginalis* Infestation in Women: a Preliminary Report**
E. REES. *British Medical Journal* [*Brit. med. J.*] **2**, 906–909, Sept. 24, 1960. 3 refs.

This paper from the Liverpool Royal Infirmary describes the results of treatment with metronidazole in 39 female patients suffering from infestation with *Trichomonas vaginalis*. The drug was given by mouth in a dosage of 600 mg. a day for 7 days to the patients and, to prevent re-infection, to their male partners. There was prompt clinical improvement within a week in the 14 cases of acute infestation, negative cultures (in Feinberg–Whittington liquid liver medium) being obtained after 12 weeks. Most of the 19 patients with subacute infestation were cured by the end of the course, with negative cultures within 12 weeks, but 3 of these did not become symptom-free; re-infestation with *T. vaginalis* and gonococci occurred in one patient, one had a persistent discharge associated with an infection by *Candida albicans*, and one did not show any clinical response to treatment, though a culture positive for *T. vaginalis* was obtained during the 8th week of observation. The remaining 6 patients were asymptomatic carriers and all except one, who was re-infected in the 6th week, were free from the parasite 12 weeks after starting treatment. Five patients complained of nausea, and a rash developed in one.

It is concluded that metronidazole is an effective remedy, although it is too early to assess its long-term value. A warning is given that the rapid disappearance of vaginal discharge after treatment may delay the diagnosis of co-existing gonorrhoea. *Janice Taverne*

697. **Treatment of Trichomoniasis with Metronidazole**
M. MOFFETT and M. I. MCGILL. *British Medical Journal* [*Brit. med. J.*] **2**, 910–911, Sept. 24, 1960. 3 refs.

Metronidazole was given to 42 female patients attending out-patient clinics for the treatment of venereal disease in Glasgow who had vaginitis due to *Trichomonas vaginalis*. The first 14 patients received 600 mg. by mouth daily for 10 days and one 0·5-g. pessary each night during that period, the next 24 received the same oral dosage but no pessary, and the remaining 4 were given the oral dosage for 7 days only. Complete relief of symptoms and absence of trichomonads on culture in Feinberg–Whittington medium indicated cure in 40 of the patients. In one patient who was given both tablets and pessaries there was no response even after further treatment for 10 days, and in another who had a very heavy infestation there was a relapse after 7 days' treatment. Of the 42 patients, 6 were pregnant. The presence of a cervical erosion did not interfere with the results, but it was noted that in 3 patients infection due to *Candida albicans* became more troublesome when *T. vaginalis* was controlled.

None of the patients has yet been observed for longer than 3 months, but the authors consider that the results justify a more extensive trial of the drug and that systemic administration is sufficient without local treatment.
Janice Taverne

698. **Certain Epidemiological, Clinical, and Diagnostic Aspects of Trichomoniasis in the Male.** (Некоторые вопросы эпидемиологии, клиники и диагностики трихомониаза у мужчин)
N. S. LJAHOVICKIJ. *Советская Медицина* [*Sovetsk. Med.*] **24**, 87–92, Sept., 1960. 16 refs.

Trichomoniasis is an important venereal disease which, in the male, is more common in the sexually active period of life and clinically presents in a great variety of forms, ranging from the acute to the asymptomatic. In the present study 190 infected males were divided into three groups suffering respectively from (1) the acute form (4·7%), (2) the subacute or chronic form (60·4%), and (3) the asymptomatic form (33·8%); a fourth group consisted of 2 healthy asymptomatic carriers. In Group 3 the diagnosis was made on the finding of trichomonads in the urine during a routine examination for other reasons. All these patients had a low-grade chronic urethritis. It is urged that clinical investigation should always include microscopical examination of stained and unstained smears of the urethral discharge, urine, secretions of the prostate and seminal vesicles, and mucosal scrapings.

Cultural methods and microscopical techniques gave positive results in 77·7% and 83·3% of these cases respectively, the former being thus a useful adjuvant to the latter. Complement-fixation tests showed no advantages and were found to be unsuitable. In 10·3% of the cases repeated laboratory examination was necessary. In 8 cases the parasite was demonstrated in urethral scrapings and prostatic secretion but not in the urine, in 9 cases in the urine and prostatic secretion but not in scrapings, in 34 cases in mucosal scrapings and urine but not in prostatic secretion, and in 14 cases in the urine only. In 5 patients with non-gonococcal urethritis the parasite was found in the material obtained under direct vision from lacunae and Littré's glands during urethroscopy, although in 3 of these cases it could not be identified in the urine, the prostatic secretion, or urethral scrapings. *S. W. Waydenfeld*

699. **The Effect of Added Calcium on Treponemal Immobilization**

F. W. Chorpenning and D. B. Beers. *Journal of Immunology* [*J. Immunol.*] **85**, 240–243, Sept., 1960. 17 refs.

The enhancing effect of optimal concentrations of calcium ion (Ca^{++}) on immune haemolysis has been known for some time. If this is due to protective action or "sparing" effect on complement component C'_1 it should be as effective in specific (immune) immobilization as in complement fixation. In order to examine this hypothesis experimentally quantitative treponemal immobilization (T.P.I.) tests were performed, with and without added Ca^{++}, under rigidly controlled conditions of time and temperature and concentrations of antigen, antibody, and C′. The titres so obtained were compared to ascertain whether the addition of calcium caused an increase. In addition, complement titrations in terms of $C'H_{50}$ activity were performed on the test mixtures at the beginning and the end of the test period.

When complement concentrations and other factors were the same, immobilization titres were consistently increased by the addition of ionic calcium. This effect was accompanied by the presence of increased haemolytic activity in the residual test mixtures after incubation. The addition of calcium had no adverse effects on the results of the T.P.I. test or on treponemal survival.

R. R. Willcox

700. **Results of Treatment of Syphilis with a Prolonged Course of Penicillin Totalling 14.4 Mega Units.** (Über Resultate der Penicillinbehandlung der Syphilis mit einer protrahierten Kur von 14,4 Millionen Einheiten)

V. M. E. Obeid-Ruggli. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **90**, 820–826, July 30, 1960. 16 refs.

This paper from the University of Zürich reports the results of treating 107 syphilitic patients with a protracted course consisting of 3 intramuscular injections, each of 600,000 units of procaine penicillin, weekly for 8 weeks, making a total dose of 14·4 mega units of the drug. The series included 20 cases of primary syphilis, 21 of secondary syphilis, 47 of latent infection, 3 of symptomatic tertiary syphilis, 5 of late congenital syphilis, and 11 of neurosyphilis. The patients suffering from neurosyphilis received preliminary bismuth injections before starting the course of penicillin. Follow-up ranged from 3 to 10 years and during this period no clinical relapses were observed. All the cases of primary and secondary syphilis were clinically cured and the serological tests became normal in those which were initially sero-positive; in the cases of late syphilis reversal did not always occur [as would be expected—as titre estimations were not carried out assessment of the results of treatment in these cases, and especially in those of latent syphilis, is difficult or impossible.]

Follow-up of the cases of neurosyphilis was incomplete and some of the patients received more than one course of treatment. In those in whom the cerebrospinal fluid was examined after treatment there was marked improvement in the findings or a complete return to normal. The author concludes that, although an observation period of 3 to 10 years is insufficient for ultimate conclusions to be drawn, this form of protracted penicillin therapy is justified in the treatment of syphilis, whether it be of the early infectious form or late syphilis. He recommends that in cases of neurosyphilis the treatment should be repeated on one or two subsequent occasions.

R. D. Catterall

701. **Validity of Reports of Penicillin-resistant Gonococci**

E. J. Gangarosa and S. G. Cary. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 1808–1810, Aug. 20, 1960. 16 refs.

There have been a number of reports recently of an increasing incidence of penicillin-resistant gonococci. The present authors examine the evidence and urge restraint and caution in diagnosing penicillin-resistant gonorrhoea. They recall the observations of DeBord (*J. Lab. clin. Med.*, 1943, **28**, 710) on a species of bacteria, *Mimea*, so-called because it is capable of mimicking the gonococcus, particularly if too much reliance is placed upon recognition of *Neisseria gonorrhoeae* by the Gram-staining reaction. None of the most recent reports have specifically excluded mimeae from bacteriological studies. Deacon (*J. Bact.*, 1945, **49**, 511) confirmed DeBord's findings by isolating mimeae from cases of so-called "penicillin-resistant" gonococcal infection, while Hughes and Carpenter (*Amer. J. Syph.*, 1948, **32**, 265) found that 91% of patients invalided out of the army because of infection with penicillin-resistant gonorrhoea had a urethritis from other bacterial causes. Indeed, these authors also demonstrated that the remaining cases of true gonococcal infection were in fact re-infections and that all the 6 strains of gonococci tested for penicillin sensitivity were inhibited by 0·08 unit of the antibiotic or less. Their observations were confirmed by Cohn *et al.* (*Amer. J. Syph.*, 1949, **33**, 86), who suggested that some cases of resistance were due to the walling-off of the sites of infection, so that a higher dosage of penicillin was necessary to ensure adequate penetration.

The authors conclude that the case for true penicillin-resistant gonorrhoea is not yet proven, and that penicillin is still the treatment of choice. *Allene Scott*

Tropical Medicine

702. Histologic Examinations of Tissues of Children with Healed Primary Lesions of Leprosy: Report of Seven Cases

J. O. NOLASCO, C. B. LARA, and J. L. IGNACIO. *International Journal of Leprosy* [*Int. J. Leprosy*] **29**, 133–139, April–June [received Oct.], 1960. 7 refs.

This report records wholly negative histologic findings in the healed skin lesion sites, regional lymph nodes, peripheral trunk nerves, and testes examined, in 7 children, born at Culion [Palawan, Philippines] of leprous parents, who died at an average age of 12 years 5 months (range 9 years 11 months to 16 years 2 months), or after an average interval of 10 years 9 months from the appearance of lesions to the time of death, and an average interval of 8 years 4 months after the apparent healing of all skin lesions. The average age at onset was 1 year 6 months. The negative clinical picture as regards signs of leprosy for an average of more than 8 years before the time of death was confirmed post mortem by the negative histologic and bacteriologic findings in the tissues examined.

Comment is made on the impracticability of searching all of the skin, lymph nodes and other structures which might still afford lodgment for any lurking latent infection. Nevertheless, we consider that the method of study, together with the regular clinical observations and concurrent laboratory findings, sufficiently justifies the opinion that the first leprosy infection in these children had been completely overcome.—[Authors' summary.]

703. Electrolyte Patterns in Cholera during Treatment: a Study of Twenty-four Cases

M. KRUATRACHUE, R. BURI, V. PHANICH, T. HARINASUTA, M. TRISHNANANDA, S. KOCHASENI, and U. PLENGVANIT. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **54**, 258–266, Oct., 1960. 2 figs., 6 refs.

During the second cholera epidemic in Thailand in 1959 the authors studied 24 patients (10 males and 14 females aged 17 to 47 years) to determine the electrolyte distribution in cholera during treatment. All the cases were acute and had been admitted to Siriraj Hospital, Bangkok. *Vibrio cholerae* was isolated in only 10, but in the remainder the clinical picture was typical.

Immediately after their admission to hospital 15 ml. of venous blood was taken to determine serum K, Na, and Cl levels and plasma specific gravity. All patients received isotonic saline intravenously for 24 hours, the amounts depending on the plasma specific gravity and the estimated losses in stools and vomit; the actual amounts given varied from 4 to 10 litres. As soon as the acute phase ended the course of the illness was divided into: (*a*) acute stage—with diarrhoea persisting although the patient had recovered from shock: here isotonic saline was continued; and (*b*) " convalescent "—where diarrhoea had stopped, whether the patient could take fluids by mouth or not: here all were given glucose (5% solution in distilled water) intravenously, since they still showed some dehydration. All patients were kept as closely as possible to physiological fluid balance, and all entering the " convalescent " stage were given potassium-containing tablets by mouth in addition (dosage 4 g. daily).

Only 10 of the patients required saline infusion after the 2nd day, and by the 5th day this was no longer necessary. In 11 cases glucose was given intravenously on the 2nd day, and in most of these it was continued till the 5th day. By the 8th day no intravenous treatment was necessary for any patient. Six patients were sufficiently recovered to be discharged by the end of the 6th day, the longest period in hospital being 20 days. There were no deaths.

Although the serum K level was very low in some cases, none showed clinical hypokalaemia; return to normal levels took some days. Serum Na followed roughly the same pattern as K, with an initial fall in level after the 2nd day, but a return to normal by the 5th day. A remarkable feature was that the serum Cl level, even in the acute stage, rarely fell below normal limits despite obvious losses in stools and vomit. Studies of the electrolytes in faeces and urine in 5 cases showed that the fluid lost in the stools on the 1st day varied from 1 to 4 litres; in some cases the electrolyte levels proved to be lower after the 1st day and the losses of K and Na were not proportionate. In the urine the concentration of K and Na was below normal in all but 2 cases.

The findings of the study can be summarized as follows. (1) The serum K level was low in acute cases and showed a fall from the 2nd day; it remained low for some time even when additional KCl was given by mouth. (2) During the first 4 or 5 days of treatment with isotonic saline or intravenous glucose the serum levels of Na and Cl fluctuated as losses continued. (3) In addition to the evident electrolyte loss in the stools, losses continued in the urine in both acute and convalescent stages. (4) Most patients recovered by the 6th to 10th day, but serum electrolyte concentration was below normal even in the presence of apparent clinical improvement. The authors consider that if additional KCl is given by mouth as soon as the patient can take it a shorter convalescent period may be possible.

W. K. Dunscombe

704. The Treatment of Amebiasis with Paromomycin (" Humatin ")

H. P. DOONER. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] 7, 486–489, Aug., 1960. 4 refs.

Paromomycin was tried in the treatment of intestinal amoebiasis in 32 adult out-patients at the Hospital San Borja, Santiago, Chile. All the patients had had symp-

toms for months, sometimes years; no healthy or asymptomatic cyst passers were included. The condition was diagnosed following examination of 6 serial stool specimens and sigmoidoscopy. The drug was given in capsules containing 250 mg., the dosage being 5 capsules daily for 5 days.

There was symptomatic improvement in all the patients from the second day of treatment, although moderate diarrhoea persisted in 11 until the drug was stopped. Slight abdominal pain occurred during treatment in 8 cases and transient leucopenia was seen in 4, but this was considered to be coincidental. No relapses were observed. All the patients were followed up for one month after treatment, 27 for 3 to 6 months, and 4 for one year, all being seen at monthly intervals. The author states that a chronic mild type of amoebic infection, not the massive acute infection of 20 years ago, is most commonly seen in Chile to-day. *P. T. Main*

705. **Intestinal Amoebiasis, with Reference to 600 Cases.** (Amibiase intestinale. Réflexions cliniques à propos de 600 observations)
H. Félix, J. Turpin, B. Desbuquois, and C. Mion. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 2096–2104, Aug. 4–12, 1960.

The authors report the clinical findings in 600 cases of intestinal amoebiasis admitted to the Hôpital Militaire Baudens, Oran, Algeria. Most of the patients were young French soldiers serving in North Africa, although some had seen previous service in the Far East or other tropical regions and had been treated inadequately. The 600 cases comprised 430 primary attacks, 82 relapses, and 88 chronic amoebic infections. Primary attacks rarely occurred in recruits during their first 3 months in North Africa, but were common after 6 to 12 months of service, the most frequent source of the infection being in the ports and urban centres of the coastal region. Dysentery was precipitated by the disturbance of the normal intestinal flora resulting from a change of diet or climate, by stress, or by the administration of sulphonamides or antibiotics. The clinical signs and symptoms observed are described in great detail. In 60% of the cases the main signs were dysentery, diarrhoea, and abdominal pain; in 14·5% the presenting symptoms were typical of gastric or gall-bladder dysfunction and in 8% were typical of a urinary disorder. Loss of weight, anorexia, and weakness were common. The diagnosis was based on the history, clinical examination (in which palpation of the colon is regarded as of prime importance), examination of the stools for amoebae, and the results of sigmoidoscopy. The difficulties presented by chronic intestinal amoebiasis are discussed. *L. G. Goodwin*

706. **Sigmoidoscopy in Amoebiasis.** (Données rectoscopiques dans l'amibiase)
C. Mion, J. Turpin, and H. Félix. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 2105–2108, Aug. 4–12, 1960.

In this second paper [see Abstract 705] the authors emphasize that in amoebiasis sigmoidoscopy is indispensable for the assessment of the condition and progress of the amoebic lesions during treatment and is also of value in prognosis. They describe the lesions revealed by sigmoidoscopy in 460 of the 600 cases investigated and attempt to correlate the appearances observed with the clinical condition of the patient. Mucosal congestion, ranging from slight reddening to dark purple ecchymoses, and areas of mucosa which appeared to have lost their "polish" were noted. The roughened areas were frequently oedematous and were painful and bled easily. Patches of purpura were often the precursors of amoebic ulcers, small purpuric areas developing into superficial erosions, while large areas formed extensive purulent ulcers. Less frequently classic amoebic ulcers undermining the mucosa and having the appearance of furuncles were seen.

The non-specific signs and the ulcers usually resolved within 8 days in response to treatment with emetine. If, after 3 or 4 courses of emetine, "unpolished" areas of mucosa remain, the authors recommend energetic treatment with the alkaloids of *Holarrhena* and administration of enemas of bismuth subnitrate and other medicaments. They conclude that a persistently congested mucosa with granular, scarred, and atrophic areas usually carries an unfavourable prognosis and that patients with severe, extensive ulceration should be treated immediately with emetine. Antibiotics given at this stage are regarded as extremely dangerous.
L. G. Goodwin

707. **Conditions for Success in the Treatment of Amoebiasis.** (Conditions des succès thérapeutiques en matière d'amibiase)
H. Félix, B. Desbuquois, J. Lescure, S. Geïer, and J. Cotton. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 2108–2114, Aug. 4–12, 1960.

This third paper on amoebiasis in North Africa [see Abstracts 705 and 706] summarizes the authors' experience in the treatment of more than 1,000 patients with this disorder seen over a period of 18 months. They emphasize that treatment must be given as early as possible and continued for 6 to 24 months, even if the patient feels well, since the amoebae must be eliminated and a beneficial flora maintained in the intestine. It is important that scarring of the bowel wall, which involves the nerve plexuses and may lead to chronic illness with psychosomatic complications, should be reduced to a minimum.

Emetine is regarded as essential for the initial treatment, and in this series the drug was given subcutaneously for 10 days in a dosage of 80 mg. daily, associated with 1 mg. of strychnine. In addition patients received every other day 100 mg. of aneurin (vitamin B_1) or 5 mg. of deoxycortone acetate. Slight side-effects were observed one hour after the 3rd, 4th, and 5th injections of emetine, while after the 7th injection a feeling of weakness and heaviness of the limbs occurred in most patients and the blood pressure fell. These effects usually disappeared 4 to 8 days after the end of treatment. Complete rest in bed was essential to minimize side-effects and to ensure maximum efficacy of the treatment. In elderly patients, alcoholic patients, and those with myocardial deficiencies the emetine was given

in doses of 40 mg. twice a day. Women were not treated during pregnancy, and no more than three courses of emetine were ever given to any one patient. The authors gave *Holarrhena* alkaloids to 65 patients who failed to respond to emetine or who had amoebic infection of the liver.

Antibiotics are not recommended until after the beginning of treatment with emetine, and when given should be supplemented with vitamins and preparations of lactic-acid-producing organisms. Enemas containing penicillin, chiniofon, bismuth subnitrate, and cod-liver oil are strongly advocated for consolidation of the treatment and for the management of chronic amoebiasis. The authors also comment upon the virtues of various iodoquinoline derivatives, arsenicals, opium, antispasmodics, vitamins, and other adjuvants and discuss in detail the management of the different forms of intestinal amoebiasis which are encountered. A polypharmaceutical supportive treatment is advised and details are given of the various French proprietary drugs available for this purpose. *L. G. Goodwin*

708. **Relationship between Malarial Parasitaemia and Symptoms of the Disease: a Review of the Literature**
G. COVELL. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **22**, 605–619, 1960. Bibliography.

709. **The Treatment of Onchocerciasis**
J. K. T. CHERRY. *East African Medical Journal* [*E. Afr. med. J.*] **37**, 550–558, Aug. [received Oct.], 1960. 32 refs.

The author of this paper from the Uganda Medical Service reviews the literature on the treatment of onchocerciasis by surgical removal of palpable nodules containing the adult worms, by administration of diethylcarbamazine or suramin, or by a combination of both methods. He then describes his own experience with these drugs in an area on the east bank of the Nile where 68% of a total of 485 inhabitants were shown by skin snips to be heavily infested with the adult *Onchocerca volvulus*. In 40 further patients nodules were present, although skin snips were negative. The author states that since only one snip was examined from each individual it is probable that the incidence of infestation was even higher.

A total of 276 patients with positive skin snip were given suramin by weekly injection (0·5 g., then 1 g.). The minimum dosage aimed at was 7·5 g., but after 2·5 g. had been given the number of patients attending fell markedly, and relatively few finished the 8-week course. Since suramin is slow in its microfilaricidal action treated patients were not re-examined until 10 months later. The cure rate appeared to be related to the amount of suramin received—for example, only 26·7% of patients given 0·5 g. were negative compared with 58·3% of those who had received 4·5 g. and 80% of those who stayed the course and received 7·5 g. The results were regarded as satisfactory at the 4·5-g. dose level, but beyond this undesirable reactions were almost invariable.

A course of suramin to a total of 4·5 g. followed by a course of diethylcarbamazine, with prednisolone to control allergic reactions, was given to 60 affected patients, all of whom were kept in bed. The regimen for the diethylcarbamazine course was as follows. After breakfast 10 mg. of prednisolone was given and half an hour later the patient was given 12 tablets, each of 50 mg., of diethylcarbamazine and told to swallow these before the midday meal, spreading the dosage as evenly as possible. This procedure was repeated after the midday and evening meals and continued for 3 days. With this routine allergic reactions were reduced to a minimum; the prednisolone was tapered off on the fourth and fifth days. At least 4 skin snips from each patient were examined immediately after treatment, these being positive in only 4 of the 60 cases. Of 17 patients followed up for 3 months, skin snips were positive in only one; skin snips were positive in none of the 8 patients examined at 6 months and in one of 8 examined after 12 months. Of the 4 patients with positive skin snips immediately after cessation of treatment, all became negative a few days later.

The author concludes that treatment with a combination of suramin and diethylcarbamazine offers a better chance of cure than with suramin alone, although diethylcarbamazine acts primarily on the larvae and suramin on the adult worms. He points out, however, that there is no room for complacency in the treatment of onchocerciasis, which still presents many difficult problems. *P. T. Main*

710. **TWSb in Treating Urinary Bilharziasis in Egyptian Children**
S. AWWAAD, H. F. NAGATY, M. ELGUINDY, and M. A. RIFAAT. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **63**, 204–205, Sept., 1960. 7 refs.

The results obtained with sodium antimony-α:α'-dimercaptosuccinate (TWSb) in the treatment of urinary bilharziasis in children are reported in this paper from Ain-Shams University, Cairo. The drug was given to 20 children aged 6 to 13 years in five intramuscular injections to a total dose of 40 mg. per kg. body weight. The dose regimen varied, one group receiving a daily injection for 5 successive days, a second group receiving an injection on alternate days, and a third group an injection twice weekly. The patients were followed up for more than 2 months. All except one of the patients were cured, there being a relapse in one patient given 5 successive daily doses. Toxic symptoms were rare and not severe and were less apparent in patients whose treatment extended over 14 days. Vomiting was the commonest side-effect, but in a small group of 4 patients not included in the series oral administration of 0·25 g. of mercaptosuccinic acid 15 minutes before injection appeared to prevent vomiting. The electrocardiogram showed marked changes in all cases, but tended to return to normal. No pulmonary reactions were evident on x-ray examination and cough was absent. The authors recommend a course of twice-weekly injections since this appears to be equally effective, safer, and less likely to be followed by relapse than are the more intensive courses. *O. D. Standen*

Allergy

711. **Prolonged Steroid Therapy in Childhood Asthma**
J. P. ANDERSON. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **100**, 341–352, Sept., 1960. 1 fig., 29 refs.

In this paper is described a study at the Leicester Chest and Isolation Hospital of the problems associated with the long-term steroid therapy of childhood asthma. The study covered 39 children under 15 years of age who had received daily treatment with prednisolone for at least 12 of the previous 15 months. Their asthma had been severe enough initially to disrupt their school and home life during the previous year, and they had failed to respond to other methods of treatment. Precipitating factors were usually multiple and included respiratory-tract infection (36) and emotional stress (29). Assessment was based on records of the number of attacks of asthma, presence of dyspnoea between attacks, school attendance, and results of physical examination, and patients were graded into 6 categories according to the severity of signs and symptoms.

The dosage of prednisolone varied, but roughly 1 mg. per year of age per day was given. During examinations or at times of stress the usual dose was increased by 5 or 10 mg. for several days, but no child received more than 20 mg. per day. After a minimum of one year's treatment withdrawal of prednisolone was attempted, the daily dose being reduced by 2·5 mg. in successive weeks. Symptomatic treatment was increased if necessary. A number of children received injections of corticotrophin, and short courses of other steroids were given from time to time.

By September, 1957, after a total experience of 538 "prednisolone-months", 8 results were classified as "excellent", 23 as "good", and 7 as "fair". One boy had died after 8 months' treatment. In sum, "over 80% of these children, previously disabled to a varying degree, were enabled to lead normal lives". Unrecognized low-grade respiratory infection often led to relapse requiring antibiotic therapy and temporary increase of prednisolone dosage. In 2 cases serious psychological stress led to deterioration, but in most cases improvement was well maintained throughout the year. Eczema usually improved and allergic rhinitis was always relieved.

During the 17 months from October, 1957, withdrawal of prednisolone was attempted; 8 children were weaned completely, but 19 still needed steroid therapy almost continuously, while 11 needed it from time to time. The apparent relationship between steroid requirement and initial severity was confirmed by the finding that 11 of the 13 children most severely affected continued to need regular maintenance treatment.

Complications of treatment included one death from unsuspected bronchopneumonia and one case of transient adrenal failure after discontinuing treatment. Infections, especially of the respiratory tract, were common. Frank obesity developed in 7 children and moon-face in 8, while suppression of growth occurred in 3 cases and was suspected in 4 others.

The author points out that when instituting steroid therapy in childhood asthma the risk of silent infections and of sudden adrenal cortical failure under stress must be constantly borne in mind. Any apparent retardation of growth should be countered by reduction in dosage below the critical level, and this must be done before the age when further skeletal growth is precluded by closure of the epiphyses. The difficulty of weaning patients after long-term steroid treatment is discussed, and in this connexion the importance of the development of steroid dependence is stressed. It is suggested that such dependence has a pharmacological rather than a psychological basis. The author concludes that long-term steroid treatment is justified in children disabled by asthma who have failed to respond to routine measures, but he emphasizes the need for expert clinical selection and regular supervision.

[The relatively small incidence of side-effects is encouraging, but it must be stressed that the ultimate effect of steroid therapy when continued over many years is still uncertain, and particularly its effect on bone metabolism. The author's findings confirm that the life of the child with severe chronic asthma can be transformed by steroid therapy over a limited period of observation.] *R. S. Bruce Pearson*

712. **Respiratory Antigen Injections. Absorption Studies by Immunologic and Radioactive Methods**
S. M. FEINBERG, H. I. RABINOWITZ, J. J. PRUZANSKY, A. R. FEINBERG, and A. KAMINKER. *Journal of Allergy* [*J. Allergy*] **31**, 421–432, Sept.–Oct., 1960. 4 figs., 5 refs.

The use of pollen extract emulsified in mineral oil as a repository injection has been reported to be of value in the desensitization treatment of patients who are allergic to ragweed.

This communication from Northwestern University Medical School, Chicago, describes investigations which were designed to investigate the safety, efficacy, and mechanism of its action. The reactivity of ragweed pollen extract emulsified with mineral oil, as estimated from the reaction to its subcutaneous injection, varied, but it was found that about 50 to 100 times the amount of allergen could be given to a ragweed-sensitive patient than would be tolerated by him if the allergen were in aqueous solution. When the extract was made radioactive by the incorporation of ^{131}I, emulsified, and injected into 3 non-allergic subjects 80% of the radioactivity disappeared from the injection site within 3 weeks, while on injection into 2 allergic subjects the same percentage disappeared within

6 to 13 days. If the radioactive aqueous extract was used without emulsification 80% of the radioactivity disappeared from the injection site within 24 hours. Of 6 non-allergic subjects who were given 10,000 units of the emulsified pollen extract, 5 showed a positive delayed reaction to skin tests for up to 3 months after the injection.

H. Herxheimer

713. **Respiratory Antigen Injections. Preparation and Therapy**

A. R. FEINBERG, S. M. FEINBERG, and E. W. FISHERMAN. *Journal of Allergy* [*J. Allergy*] **31**, 433–440, Sept.–Oct., 1960. 20 refs.

The investigations described in the previous paper [Abstract 712] were followed by a study of the clinical value of emulsified pollen extracts. Doses of 500 to 6,000 units of ragweed pollen extract emulsified in mineral oil were given to 26 patients with ragweed hay-fever in one or 2 intramuscular injections. After this treatment the results of skin, eye, and nose tests with ragweed extract remained ambiguous and the effect had therefore to be assessed from the subjective impressions of the patients and their need for additional medication. The results were judged to be " excellent " in 4 cases, " good " in 13, " fair " in 2, and " poor " in 5, 2 cases not being followed up.

These results are regarded as encouraging, but are not so good as those reported from Boston by Brown (*Ann. Allergy*, 1958, **16**, 353 and 510; 1959, **17**, 34 and 358). It is suggested that the difference might be due to the greater prevalence of ragwood pollen in the Chicago area than in Boston. *H. Herxheimer*

714. **Studies on the Relationship of the Release of Serotonin and Histamine, by Chemical Means, to Anaphylaxis in the Rabbit**

T. P. WAALKES and H. COBURN. *Journal of Allergy* [*J. Allergy*] **31**, 395–405, Sept.–Oct., 1960. 4 figs., 27 refs.

A variety of substances were tested at the National Heart Institute, Bethesda, Maryland, both *in vitro* and *in vivo* to determine whether any of them were capable of causing anaphylactoid reactions or the release of histamine in rabbits. When rabbit whole blood was incubated with glycogen, starch, antigen–antibody complex precipitate, trypsin, or egg albumen serotonin and histamine were released from the platelets into the plasma; the same occurred when the antigen was added to the blood of rabbits sensitized to horse serum. The concentrations of serotonin and histamine in the whole blood and in the lungs of normal rabbits were studied before and after the intravenous injection of proteose peptone, peptone, trypsin, glycogen, and antigen–antibody precipitate. It was found that the injection of glycogen, but of none of the other substances, reproduced exactly the changes in serotonin and histamine concentrations (and in the platelets) which occurred after the injection of antigen–antibody complex or during anaphylactic reactions in sensitized rabbits. In experiments *in vitro* it was found that the addition of ethylenediamine tetraacetate (EDTA) prevented the release of serotonin histamine from the blood of a sensitized rabbit when antigen was added. It is suggested that this inhibition is caused by the lack of ionized calcium in the blood in the presence of EDTA. *H. Herxheimer*

715. **Seasonal Treatment of Pollinosis by Cutaneous Application of Allergens after Scarification.** (Traitement co-saisonnier de la pollinose par applications cutanées d'allergènes après quadrillage)

N. T. KY and C. LAROCHE. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 2374–2376, Sept. 18. 1960. 4 refs.

During the hay-fever season of 1959 a method of treatment involving the application of pollen extract to scarified rectangular areas on the forearm of 22 patients was investigated at the Hôpital Cochin, Paris. Without drawing blood the forearm of each patient was marked with 20 horizontal scratches 5 cm. in length and 10 vertical scratches 10 cm. in length, these being separated by a distance of 5 mm. Pollen extract, in a concentration previously determined by the results of skin tests, was then applied to the rectangular areas thus formed. This was followed by local erythema and oedema persisting for up to 24 hours. If the symptoms of hay-fever improved the procedure was repeated 7 to 10 days later; if they did not improve this was done 3 days later. In 2 patients all symptoms disappeared and in 9 others sneezing or nasal obstruction persisted in spite of some improvement. In the remainder, however, there was little or no change. The authors regard the method as less satisfactory than the usual intracutaneous injection with increasing amounts of allergen extract.

H. Herxheimer

716. **Some Biochemical Characteristics of Allergic Histamine Release from Leukocytes of Ragweed-sensitive Subjects**

E. MIDDLETON JR., W. B. SHERMAN, W. FLEMING, and P. P. VANARSDEL JR. *Journal of Allergy* [*J. Allergy*] **31**, 448–454, Sept.–Oct., 1960. 11 refs.

When ragweed antigen is added to heparinized whole blood from ragweed-sensitive patients histamine is released from the leucocytes into the plasma. In experiments reported from the College of Physicians and Surgeons, Columbia University, and the University of Washington School of Medicine the amount of histamine so released was measured by the method of Lowry *et al.* (*J. Pharmacol. exp. Ther.*, 1954, **112**, 116) and the influence of various agents on its release was studied. When oxalate, citrate, or ethylenediamine tetraacetate was added in anticoagulant concentration the release of histamine was inhibited, but this did not occur if calcium chloride had been added beforehand. Chelating agents, iodoacetate, phenol, phenylbutazone, and phthalate also acted as inhibitors, while salicylate, fluoride, cyanide, azide, and urethane did not. Temperatures above 45° C. inhibited the release of histamine completely, while temperatures below 37° C. reduced the amount released.

H. Herxheimer

Nutrition and Metabolism

717. **Some Diseases Associated with Protein Malnutrition, as Seen in Jamaica**
E. P. TAXAY. *Gastroenterology* [*Gastroenterology*] **39**, 173–177, Aug., 1960. 12 refs.

Three diseases which occur in Jamaica, akee poisoning, veno-occlusive disease, and kwashiorkor are described. It is thought that previous protein malnutrition is necessary for these diseases to appear.—[Author's summary.]

718. **The Absorption of Folic Acid and Labelled Cyanocobalamin in Intestinal Malabsorption. With Observations on the Faecal Excretion of Fat and Nitrogen and the Absorption of Glucose and Xylose**
A. DOIG and R. H. GIRDWOOD. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 333–374, July [received Sept.], 1960. 3 figs., bibliography.

At the Royal Infirmary, Edinburgh, the absorption of folic acid, labelled cyanocobalamin, glucose, and xylose and the faecal excretion of fat and nitrogen have been studied in 65 patients with intestinal malabsorption and in 50 control patients, of whom 25 had Addisonian pernicious anaemia. The intestinal malabsorption was of the sprue type in 30 patients, of whom 26 (83%) showed impaired folic acid absorption and 40% impaired cyanocobalamin absorption, the latter defect being usually, but not invariably, accompanied by the former. These patients also usually showed impaired absorption of glucose and xylose and all of them had poor absorption of either glucose, xylose, or folic acid. In 20 cases the features of intestinal malabsorption followed gastric operation; of these, 14 showed impaired cyanocobalamin absorption with achlorhydria, which, however, improved in all on treatment with intrinsic factor. None of this group showed decreased absorption of folic acid, although in 10 there was increased faecal fat excretion. The degree of malabsorption of cyanocobalamin was less than that found in patients with Addisonian pernicious anaemia.

Of the 15 patients who had intestinal malabsorption associated with an anatomical lesion of the small intestine, the absorption of cyanocobalamin was impaired in 13, but only 3 had any defect of folic acid absorption. In cases in which stagnation occurred within the lumen of the small bowel temporary improvement in cyanocobalamin absorption followed administration of a tetracycline antibiotic. Improvement also followed surgery, except in 3 cases in which 90 to 150 cm. of the lower ileum had been resected. Organisms isolated from stagnant areas of the small intestine were shown to take up cyanocobalamin from the medium and to synthesize folic acid. Evidence is presented to show that the jejunum is the principal site of folic acid absorption and the ileum the main site of cyanocobalamin absorption. Study of the absorption of these substances is considered to be of considerable diagnostic value in cases of intestinal malabsorption. Illustrative case histories are given, the detailed findings tabulated, and the results obtained are fully discussed. *F. W. Chattaway*

719. **Correlation of Radioactive and Chemical Faecal Fat in Different Malabsorption Syndromes**
B. D. PIMPARKAR, E. G. TULSKY, M. H. KALSER, and H. L. BOCKUS. *British Medical Journal* [*Brit. med. J.*] **2**, 894–900, Sept. 24, 1960. 5 figs., 29 refs.

From the Graduate School of Medicine, University of Pennsylvania, Philadelphia, the authors report the results of a fat absorption test using triolein labelled with radioactive iodine (^{131}I) which was carried out on 24 volunteers and 102 patients suspected of suffering from various types of intestinal malabsorption. The diseases investigated were grouped under 8 headings, ranging from idiopathic steatorrhoea to a syndrome called "functional enterocolonopathy", and included regional enteritis, diseases of the pancreas and hepato-biliary system, and ulcerative colitis. The labelled triolein was administered orally either as an emulsion or in capsule form. Blood was withdrawn and the radioactivity measured at 2-hourly intervals until the peak activity was reached, while radioactivity in the faeces was determined until it had reached insignificant levels. Chemical faecal fat analyses were also performed. The value which was fixed as the limit of normal for the blood test was a peak of at least 9% of the administered labelled material, for the faecal test a figure of up to 7%, and that for the chemical faecal determinations at a maximum of 7 g. of fat per day.

The mean values for blood and faecal radioactivity in the control subjects differed significantly from those in all the diseases studied except ulcerative colitis and the functional group. In individual cases chemical fat analysis proved by far the most sensitive method. There was complete agreement between the two triolein tests and the chemical faecal fat estimation in 46% of the cases and complete disagreement in 13%. In spite of its limitations the authors recommend the use of the radioactive triolein test as a good, simple, exploratory technique, especially if there are no facilities for the more accurate chemical methods. *R. Schneider*

720. **Absorption and Elimination of ^{15}N after Administration of Isotopically Labelled Yeast Protein and Yeast Protein Hydrolysate to Adult Patients with Coeliac Disease. I. Rate of Absorption of ^{15}N Yeast Protein and Yeast Protein Hydrolysate**
C. W. CRANE and A. NEUBERGER. *British Medical Journal* [*Brit. med. J.*] **2**, 815–823, Sept. 17, 1960. 9 figs., 38 refs.

At St. Mary's Hospital Medical School, London, the absorption of yeast protein and its hydrolysate labelled with radioactive nitrogen (^{15}N) was studied in 4

patients with idiopathic steatorrhoea and compared with the findings in one healthy control subject. The labelled materials were given by mouth in amounts equivalent to 0·4 mg. of ^{15}N per kg. body weight in 250 ml. of water. Specimens of urine were collected at half-hourly intervals and assays of ^{15}N were carried out on urinary ammonia and urea in a mass spectrometer. It was found that after feeding the whole protein the peak appearance of the isotope in urinary ammonia was delayed by 60 to 90 minutes in the patients with idiopathic steatorrhoea compared with the healthy individual; in urinary urea this was also delayed by 90 minutes. Absorption of the labelled hydrolysate by the patients with idiopathic steatorrhoea, however, as determined by the appearance of ^{15}N in the urinary ammonia, was delayed only for 30 to 75 minutes. In these circumstances, however, the appearance of ^{15}N in the urinary urea became erratic; thus in one patient it was delayed for 30 to 60 minutes, but in the 3 others the delay ranged from 90 to 120 minutes and was therefore longer than after feeding the whole protein.

The authors suggest that a reduction in the absorptive surface of the small intestine is the main cause for the delay in absorption of the hydrolysate, while they regard a reduction in the number of mucosal cells or specific changes in their enzymic composition as the cause for the further delay in absorption of the whole protein. They also believe that disturbances of motility may play a part. [No attempt is made to explain the discrepancies in the times of appearance of the ^{15}N in urinary ammonia and urinary urea after feeding the hydrolysate.]

R. Schneider

721. **Absorption and Elimination of ^{15}N after Administration of Isotopically Labelled Yeast Protein and Yeast Protein Hydrolysate to Adult Patients with Coeliac Disease. II. Elimination of Isotope in the Urine and Faeces**

C. W. CRANE and A. NEUBERGER. *British Medical Journal* [*Brit. med. J.*] **2**, 888–894, Sept. 24, 1960. 2 figs., 25 refs.

In this second study [see Abstract 720] yeast protein and its hydrolysate labelled with ^{15}N were given to healthy subjects and to patients with adult coeliac disease by the methods previously described, the purpose of the study being to investigate the excretion of ^{15}N in the urine, to determine the origin of faecal nitrogen in both groups, and to discover the possible effects on the general metabolism of increased excretion of nitrogen in the faeces. After receiving the whole protein the combined urinary and faecal output of ^{15}N over a 3-day period was the same in the patients as in the control group. In the patients, however, the amount of ^{15}N in the urine tended to be lower and that in the faeces higher; in the patients also there was a further excretion of ^{15}N in the faeces during the second 3-day period after taking the labelled material, whereas in the controls almost all the ^{15}N had been excreted within the first 2 days. Results with the hydrolysate did not differ significantly from those with the whole protein.

Discussing the origin of faecal nitrogen the authors conclude that a major part comes from non-dietary sources in both the healthy subject and in the patient with idiopathic steatorrhoea. In the patients the increased amount of nitrogen in the faeces may possibly be due to deficient absorption of nitrogen or alternatively to a leakage of urea, amino-acids, or protein into the bowel as a result of the disorganization of the intestinal mucosal surface. [No mention is made of the contribution made by bacterial action, which amounts to about one-third of the total.]

R. Schneider

722. **Observations on Carbohydrate Metabolism in Obesity**

W. I. MORSE, J. J. SIDOROV, J. S. SOELDNER, and R. C. DICKSON. *Metabolism; Clinical and Experimental* [*Metabolism*] **9**, 666–679, July, 1960. 6 figs., 26 refs.

In the study here reported from Dalhousie University, Halifax, Nova Scotia, the results of the oral and intravenous glucose tolerance tests were compared in 12 obese female patients (mean age 38 years) whose weight had been for some years at least 30% above the mean "ideal" based on height and frame and in 5 control female patients (mean age 22·6 years) who were free from disorders known to affect carbohydrate metabolism and whose weight was within 10% of the mean ideal weight. A negative family and personal history of diabetes mellitus was required for both groups as well as freedom from evidence of hepatic and renal damage and cardiac failure. The 12 obese subjects were found to have impaired oral glucose tolerance and a slightly raised fasting blood level. However, following an intravenous glucose load these patients showed a normal net glucose removal rate and a normal rise in the blood pyruvate level.

The authors suggest that the findings indicate that a diagnosis of mild diabetes mellitus cannot be made solely on the result of an oral glucose tolerance test in the presence of obesity of long duration. After an oral galactose load the blood galactose curve in these obese females was relatively flat and the galactose removal rate after an intravenous load was increased. These results would not be expected if hepatic glycogenesis were impaired in obesity. It is concluded that all the data are consistent with the interpretation that hepatic glucose production is increased in obesity, both in the fasting and the glucose-loaded states. It is suggested that in performing intravenous glucose studies on obese patients the effects of the enlarged glucose space should be considered in calculating both the glucose dosage and the glucose removal rate. The authors conclude that "the glucose-disappearing curve is best analysed by obtaining the first derivatives and then determining the specific rate constant for glucose removal and the theoretical blood glucose concentration at equilibrium".

A. G. Mullins

723. **Idiopathic Acquired Agammaglobulinemia Associated with Thymoma: Report of Two Cases and Review of the Literature**

J. GAFNI, D. MICHAELI, and H. HELLER. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 536–541, Sept. 15, 1960. 4 figs., 39 refs.

Gastroenterology

724. **Tobacco-induced Epithelial Proliferation in Human Subject: Long-term Effects of Pipe Smoking on Epithelium of Hard Palate**
I. CHAPMAN and C. H. REDISH. *Archives of Pathology* [*Arch. Path.*] **70**, 133–140, Aug., 1960. 5 figs., 11 refs.

The long-term effects of tobacco smoke on the epithelium of the hard palate were studied at Bird S. Coler Hospital, New York, in 19 elderly men with varying degrees of leukoplakia of the hard palate discovered during routine dental examination. All 19 patients were habitual pipe-smokers. Biopsy specimens of lesions were examined histologically and compared with specimens taken from the mouths of 3 non-smokers. The histological findings were correlated with the results of clinical observation and both these were correlated with the amount of tobacco smoked and the length of time the patient had been a pipe-smoker. It is concluded that " the severity of the epithelial proliferation is suggestively related to the length of time [a pipe has been] smoked and that the heat of the pipe tobacco smoke and the total accumulated amount of tobacco smoked are not factors ".
G. Calcutt

725. **Spasmolytin in the Treatment of Chronic Gastritis and Peptic Ulcer.** (Опыт лечения спазмолитином больных хроническими гастритами и язвенной болезнью)
P. I. ŠILOV and JU. I. FIŠZON-RYSS. *Советская Медицина* [*Sovetsk. Med.*] **24**, 44–49, Oct., 1960. 14 refs.

" Spasmolytin ", an analogue of adiphenine hydrochloride, was synthetized in the U.S.S.R. in 1937. In addition to a myotropic and atropine-like effect, the drug exerts a strong central effect, has local anaesthetic properties, and blocks the parasympathetic ganglia. Of 208 patients, all males and 95% of them aged between 20 and 25 years, suffering from chronic gastritis or peptic ulcer, 156 received 0·25 g. of spasmolytin three times a day before meals for 16 to 21 days; in addition in 47 of these patients spasmolytin infiltration block was carried out every 3 to 4 days on four occasions in all, 50 ml. of a 0·5% spasmolytin solution being injected into a skin segment 5 cm. wide and 10 to 15 cm. long at the level of D 6–7 and starting 2 to 3 cm. lateral to the spine. The remaining 52 patients received no treatment (except the intravenous injection of 300 mg. of ascorbic acid daily) and served as a control group.

In the trial group the intensity of pain was greatly diminished within 5 days in 69 of the 99 patients with chronic gastritis and in 42 of the 57 with peptic ulcer. Towards the end of the course of spasmolytin the pain completely disappeared in 110 (70·5%), diminished greatly in 40 (25·7%), and persisted only in 6 (3·8%) of 156 patients; in the control group the corresponding figures were 18 (34·6%), 24 (46·2%), and 10 (19·2%). Of 30 patients with peptic ulcer given spasmolytin by mouth only, the pain disappeared in 19, while of 27 treated in addition by spasmolytin infiltration of the skin, it did so in 24. The results were least satisfactory in patients with antral gastritis. The gastric secretory function became normal in 83% of patients with either chronic gastritis or peptic ulcer. Free acid concentration returned to normal in 57% and 54% of patients with chronic gastritis and peptic ulcer respectively. In the control group the secretory function returned to normal in 69% and free acid concentration in 43% of patients. Motor function, which was abnormal before treatment in 69% of patients, became normal after treatment in 93%. The clinical improvement in the patients receiving spasmolytin was not usually accompanied by radiological improvement and in some cases the ulcer crater persisted. Oral spasmolytin gave rise to no serious side-effects, but spasmolytin infiltration was followed in a majority of patients by a state resembling inebriety lasting 15 to 30 minutes and followed by a deep sleep of 3 to 4 hours' duration, the latter being regarded as beneficial.
S. W. Waydenfeld

726. **Post-Gastrectomy Syndromes: a Review**
C. F. W. ILLINGWORTH. *Gut* [*Gut*] **1**, 183–192, Sept., 1960. 36 refs.

727. **The Increasing Incidence of Carcinoma of the Pancreas. A Clinical and Statistical Study**
H. P. LAZAR, M. A. SPELLBERG, and R. E. FOX. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **34**, 235–247, Sept., 1960. 2 figs., 40 refs.

Clinical observation having indicated that there has been an absolute increase in the incidence of carcinoma of the pancreas, the authors reviewed all the case records at Michael Reese Hospital, Chicago, for the 5 years 1952–7. During that period 79 patients with carcinoma of the pancreas were admitted. It is stated that in one of the years covered by the review (1956) 19 cases of pancreatic carcinoma were admitted compared with 24 cases of gastric carcinoma; in the other 4 years the ratio of cases of gastric carcinoma to pancreatic carcinoma was approximately 2:1.

The mean age of the 79 patients (52 male and 27 female) was 62 years (range 29 to 94 years). The commonest symptoms were loss of weight (in 57 patients), jaundice (in 36), and epigastric or back pain or both (in 53). No single laboratory or radiological examination provided adequate diagnostic data. The authors refer to the work of others who have found exfoliative cytology to have a " diagnostic accuracy of 62% ", but state that although the new method of duodenal intubation facilitates the investigation of exfoliative cytology, there is " no evidence that this technique is effective in establishing an early diagnosis ". They point out that radical surgery in the form of removal of the pancreas does not

yield good results. Simple exploration or exploration combined with biliary drainage for the relief of extrahepatic obstructive jaundice was undertaken in 70 of the patients; the mean survival time was 12 weeks.

I. McLean Baird

LIVER AND GALL-BLADDER

728. **Determination of the Aldolase Activity and Serum Protein Pattern in the Diagnosis of Botkin's Disease [Infective Hepatitis].** (Использование методов определения активности альдолазы и электрофоретического исследования белков сыворотки крови для диагностики болезни Боткина)

N. I. Makarevič, L. I. Gur'janova, and M. I. Tartakovskaja. *Терапевтический Архив* [*Ter. Arh.*] **32**, 49–51, Sept., 1960. 7 refs.

In view of the increasing importance of infective hepatitis the lack of a specific and reliable diagnostic test in the early stages of the disease is a definite drawback. Also the detection of early cases and abortive or latent forms of the disease is a most important preventive measure in the selection of prospective blood donors. In this study serum aldolase activity was determined in 50 patients and 100 healthy control subjects by a micromethod based on the condensation of the products of disintegration of 1:6-fructose diphosphate, triose-phosphates, and 2:4-dinitrophenylhydrazine, which in an alkaline medium gives rise to a colour reaction.

In the controls the serum aldolase level ranged from 2 to 10 (mean 5) units, but in patients with infective hepatitis values 4 to 5 times as great were reached during the first few days of the illness and remained high until the 20th to 30th day, when a gradual return to normal was noted. The diagnostic value of this investigation in infective hepatitis is greatest therefore in the pre-icteric stage and in the latent and abortive forms of the disease and also in examining contacts of patients with the disease. The serum protein pattern showed a marked fall in the albumin level by an average of 9·4% and a rise in that of α_1 globulin by 61%, of α_2 globulin by 25·8%, of β globulin by 19·9%, and of γ globulin by 7·8%, while the albumin:globulin ratio was reduced to 0·9. There was also a striking reduction in the albumin: α_2 globulin ratio, which was 4·5, the normal ratio being 7·3.

S. W. Waydenfeld

729. **Sodium and Water Diuresis in Cirrhotic Patients with Intractable Ascites following Chemical Inhibition of Aldosterone Synthesis**

D. A. Holub and J. W. Jailer. *Annals of Internal Medicine* [*Ann. intern. Med.*] **53**, 425–444, Sept. [received Nov.], 1960. 5 figs., 35 refs.

Su 4885 [2-methyl-1:2-bis(3-pyridyl)-1-propanone], an inhibitor of the enzyme responsible for 11β-hydroxylation within the adrenal cortex, was administered to 8 patients with hepatic cirrhosis, intractable ascites and "secondary" hyperaldosteronism. Aldosterone synthesis was effectively diminished by this compound; however, the adrenal cortex produced large quantities of 11-desoxycorticosterone (DOC) under the influence of Su 4885. The net effect of aldosterone inhibition and DOC production was continued retention of sodium and water in 7 of 8 patients. However, when suppression of ACTH release was achieved by the administration of prednisone, Su 4885 treatment resulted in inhibition of aldosterone synthesis without concurrent stimulation of DOC synthesis. Significant diuresis of sodium and water was produced by combined treatment with Su 4885 and prednisone in 3 of 5 patients. Urinary sodium excretion rose from less than 5 mEq. per day to values of over 100 mEq. per day in the patients who responded to this regimen.

It is concluded that the hypersecretion of aldosterone plays a significant role in the pathogenesis of sodium and water retention in many patients with hepatic cirrhosis and ascites.—[Authors' summary.]

730. **Emptying Effect on the Gallbladder of Tween 80.** [In English]

L. Andrén and G. Theander. *Acta radiologica* [*Acta radiol. (Stockh.)*] **54**, 17–21, July, 1960. 3 figs., 11 refs.

The authors noticed that when using "bilijodon" capsules for cholecystography the gall-bladder was stimulated to empty in a number of cases. These capsules contain the sodium salt of iopanoic acid and a combination of three solvents, of which one is "tween 80", a non-ionic wetting agent consisting of polyethylene oxide linked with the mono-oleate of sorbitane.

In order to assess the effect of these solvents special capsules were prepared filled with only one of the solvents and given to patients who on the previous day had received one of the routine cholecystographic contrast media. Two of the solvents had little or no effect, but tween 80 invariably caused a striking contraction of the gall-bladder, and in 8 of 9 patients examined the bile ducts were demonstrated. The effect of tween 80 upon the gall-bladder became maximal 30 minutes to 2 hours after the capsules had been taken. *A. M. Rackow*

731. **The Significance of Reflux of the Contrast Medium in Oral Cholecystography.** (Die Bedeutung des Kontrastmittelrückflusses in den Ductus hepaticus bei der oralen Cholecystographie)

C. Wiesser and A. Neiger. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **90**, 1083–1086, Sept. 24, 1960. 8 figs., 10 refs.

From the Cantonal Hospital, Chur, Switzerland, the authors report that of a series of 738 oral cholecystograms performed since 1956 on patients with disorders of the biliary tract, the majority showed pathological findings which were not associated with stones in the gall-bladder. They suggest that the two main radiological signs of dysfunction of the biliary tract which are relevant to the interpretation of cholangiographic findings are: a change in the emptying rhythm (that is, evacuation either too rapid or too slow) and reflux of the contrast medium into the hepatic duct. The latter is of different types corresponding to different clinical pictures, as follows. (1) Simple reflux with a normal emptying rate and no widening of the bile duct (14 cases) was associated with a history of disease of neighbouring organs, such as gas-

tritis, pyelitis, or hiatus hernia. (2) A reflux with increased rate of evacuation but no widening of the bile ducts (12 cases) was associated with cholecystitis. (3) Reflux with delayed emptying of the hypnotic gall-bladder and normal bile ducts (4 cases) was associated with appendicitis and hepatitis. (4) Reflux with normal evacuation but with a pathologically dilated bile duct (over 5 mm.) was associated with various conditions, including cholelithiasis. (5) Reflux with accelerated emptying of the gall-bladder and dilated ductus (11 cases). (6) Reflux with delayed evacuation and widening of the bile duct associated with (*a*) hypotony of the gall-bladder, and (*b*) hypertony of the gall-bladder. Of 226 patients with disturbed emptying of the gall-bladder, 69 showed reflux, of whom only 9 had cholelithiasis. Enlargement of the common duct, apart from certain exceptions, is due to some anatomical obstruction at the papillary end. *E. Forrai*

INTESTINES

732. **On the Pathogenesis of Ulcerative Colitis.** (О патогенезе язвенного колита)
J. Polcak, V. Vokurka, and M. Skalova. *Советская Медицина* [*Sovetsk. Med.*] **24**, 68–72, Oct., 1960. 14 refs.

The immunological changes taking place during the development and progress of ulcerative colitis were studied by means of Wagner's modification of the Calvelti colloidal agglutination reaction (*J. Immunol.*, 1947, **57**, 141), a total of 205 patients with various gastro-intestinal diseases being investigated. Since the reaction was positive only in the 30 patients with ulcerative colitis further specific bacteriological and serological investigations (such as the Wassermann reaction and the Coombs test) were carried out on this group only, the agglutination reaction being observed repeatedly during a period of 3 years.

The results indicated the importance of auto-immunization reactions in the development and course of ulcerative colitis and the close connexion of such reactions with the pathogenesis. The primary and decisive role in the development of the disease is attributed to the mesenchymal elements in the submucosa of the colon, the antibody titre reflecting the activity of the pathological process. If it is accepted that the course of the disease is a reflexion of immunological crises and reactions of the body as a whole, then the colloidal agglutination reactions acquire clinical and prognostic value. It was observed that after total colectomy the antibodies disappeared only if a new immunological equilibrium became established. However, in other cases in which the titre of the colloidal reaction was altered the possibility arises of various types of activity of the process. The rise of the antibody titre precedes the clinical onset of symptoms and later on can serve as an index of the effects of treatment. It is suggested that the antibodies against the colonic tissues could conceivably be formed as a result of the action of bacteria or of non-specific toxins or might follow some neuropsychological stress giving rise to vascular spasm and local ischaemia. Other possible factors are a congenital anomaly or functional changes in the enzymatic processes which take place in the wall of the colon, thus altering its biological identity, in which case the altered tissue might then act as an antigen. *S. W. Waydenfeld*

733. **Steatorrhoea in the Adult**
J. Badenoch. *British Medical Journal* [*Brit. med. J.*] **2**, 879–887, Sept. 24, 1960, and 963–974, Oct. 1, 1960. 21 figs., bibliography.

In the first of these two papers on steatorrhoea in the adult the author briefly surveys the history of the disease from the second century A.D. to the classic description by Gee in 1888 (*St. Bart's Hosp. Rep.*, **24**, 17) and then presents a review of a series of 163 personal cases seen at the United Oxford Hospitals in recent years. These are grouped under 12 headings, by far the greatest number (106) belonging to the idiopathic group. Most of these, the author claims, were cases of adult coeliac disease, as suggested by their response to a gluten-free diet, although the aetiology was not uniform in all the cases. The chief presenting symptoms were diarrhoea, abdominal distension, and flatulence. Osteomalacia occurred in 26 cases, 20 of which belonged to the idiopathic group. In some cases tetany occurred as a result of reduced calcium absorption, but hyperactivity of the parathyroid glands frequently compensated for this at the expense of the bones. Such hyperactivity occasionally proceeded to tumour formation. Haemorrhage due to lack of vitamin K occurred in 17 patients in the idiopathic group. Sore tongue was complained of by 118 of the patients, but skin rashes and peripheral neuropathy were rare. The relation of these symptoms to vitamin-B deficiency is very dubious. Loss of weight of 14 lb. (6·4 kg.) or more occurred in 76% of the patients. Several factors contributed to this; for example, not only were the intake and absorption of food reduced, but deficiencies of pyridoxine and possibly also of vitamin C might interfere with intermediate amino-acid metabolism. Disturbances of protein synthesis, as shown by an abnormal electrophoretic pattern, also contribute to the reduction in plasma protein levels, while in addition there is sometimes leakage of protein into the intestine, as shown by studies with labelled polyvinyl-pyrrolidine. Potassium depletion not only produced electrocardiographic changes and weakness of skeletal muscles, but also contributed to disturbances of intestinal motility and tone. Anaemia, microcytic, macrocytic, or mixed, was a frequent symptom and was due to failure to absorb iron, vitamin B_{12}, and folic acid. In the patients with idiopathic steatorrhoea vitamin-B_{12} deficiency was not due to lack of intrinsic factor, as in pernicious anaemia, although the patients were unable to secrete this factor during an exacerbation of the disease, the main cause being the poor absorption of the vitamin from the intestine. In patients with the blind-loop syndrome and in those with small-intestinal diverticulosis bacterial infection interfered with the absorption of vitamin B_{12}. Iron-deficiency anaemia was common and often did not respond to oral therapy, so that paren-

teral administration of iron was necessary. Of the 163 patients, 21 died, 9 of these belonging to the idiopathic group. Of the remaining 12 deaths, 3 occurred in a group of 8 patients suffering from upper intestinal diverticulosis.

In his second paper the author discusses the aetiology, diagnosis, and treatment of steatorrhoea in the adult. The possibility of coeliac disease, idiopathic steatorrhoea, and tropical sprue being due to a common genetic defect is regarded as likely, at least in regard to the first two diseases. The effect of wheat gluten in precipitating steatorrhoea is discussed in detail and it is suggested that the small group of cases of adult idiopathic steatorrhoea that do not respond to a gluten-free diet either may have progressed too far or may be of a different aetiology. The author comments on the odd fact that the histological picture in tropical sprue is so similar to that in idiopathic steatorrhoea and coeliac disease in spite of the different therapeutic response to the withdrawal of gluten. So-called fibrocystic disease of the pancreas involves not only the pancreas, but all the exocrine glands, and one ingenious theory suggests that excessive production of acetylcholine or lack of enzymes which destroy it may be a causative factor. The syndrome described by Zollinger and Ellison (*Ann. Surg.*, 1955, **142**, 709) is discussed in detail. Here the hypersecretion of hydrochloric acid by the stomach is thought to be the cause of the steatorrhoea, either by inactivating the pancreatic enzymes or by stimulating excessive secretion of mucus by the small intestine. Three causes are suggested for the steatorrhoea which follows gastrectomy: (1) absence of the natural stimulus to pancreatic secretion due to the absence of food in the duodenum, (2) inadequate mixing of food in the diminished gastric reservoir, and (3) dilatation of the afferent loop with possible stagnation of its contents. Diverticula of the jejunum and blind loops of the small intestine are frequently associated with megaloblastic anaemia and steatorrhoea; both these conditions are due to the presence of bacteria, since both respond to antibacterial therapy. Whipple's disease is attributed to a primary fault in some of the cells of the reticulo-endothelial system which results in their producing an abnormal glucoprotein instead of ribonucleic acid.

Among the diagnostic tests for steatorrhoea the author recommends daily faecal fat estimations (an accurately measured fat intake is unnecessary). The labelled triolein test is useful for rapid screening, while estimation of urinary xylose excretion is a useful measure for detecting defective absorption. Radiological examination of the small intestine is recommended in every case, although radiological changes are not confined to idiopathic steatorrhoea, but may also be found in pancreatic deficiencies. The histological examination of perorally obtained biopsy specimens of the mucosa of the small intestine is advocated as a real advance. Multiple specimens from the same patient have shown that the disease usually involves the whole of the upper small intestine, but that the ileum may be normal. Opinions on the possibility of histological recovery of the mucosa with treatment are still conflicting. The introduction of the gluten-free diet has revolutionized the treatment of idiopathic steatorrhoea. In addition to diet the author advocates "shotgun" vitamin therapy, while steroid therapy may occasionally be helpful in resistant cases, but the well-known dangers of this treatment have to be taken into consideration. Small doses of hydrochloric acid are advocated in the steatorrhoea which follows gastrectomy.

Administration of steroids and irradiation of the abdomen are suggested for the treatment of Whipple's disease. [No mention is made of the recent dramatic successes with antibacterial therapy in this disease.]

R. Schneider

734. **Changes in Enzymatic Activity in the Intestines in Dysentery.** (Некоторые показатели ферментативной деятельности кишечника при дизентерии)
I. N. Ščetinina. *Терапевтический Архив* [*Ter. Arh.*] **32**, 52–57, Sept., 1960. 26 refs.

The effect of acute and chronic dysentery on the function of the intestine results in an increase in the faecal concentration of enterokinase and, less constantly, of alkaline phosphatase. The author reports that in 36 of 42 patients with acute dysentery the faecal enterokinase content was increased from the normal value of 10 to 20 units per g. to 40 to 60 or in exceptional cases to 2,250 to 5,060 units per g. In 31 of these patients the faecal alkaline-phosphatase content increased from a normal of 200 to 500 units per g. to 1,800 to 5,060 units or even in one case to 17,000 units per g. There was no direct correlation between the rise in faecal enzyme level on the one hand and severity of the disease number and character of the stools, and recto-sigmoidoscopic findings on the other. The rise in level persisted during convalescence, while the changes in the intestinal flora occurring during treatment with sulphonamides and antibiotics and the resulting increase in enzyme production gave rise to further increase in the faecal enzyme content. Normal faecal enzyme levels were attained in only 15 of the 36 patients, so that the cure was not complete in 21.

The faecal enterokinase and alkaline-phosphatase contents were also abnormally high in 71 of 76 patients with chronic dysentery. The rise was more persistent in the presence of associated disease (such as gastritis, cholecystitis, peptic ulcer, parasitic infestation, or protozoal colitis) or of severe procto-sigmoiditis, but otherwise bore no relation to the clinical condition. Of 30 patients with chronic dysentery who were treated with sulphonamides, antibiotics, and various Russian antigenic preparations the enzymatic activity in the large intestine and the faecal enzyme content rapidly returned to normal in 5, improved in 7, and showed no change in 18. At the same time 25 of these patients were clinically cured and 5 clinically improved. Lastly, of 22 patients with chronic dysentery who were treated with antigenic preparations alone, the enzymatic activity in the colon became normal in 7, improved in 6, and was unchanged in only 7. Clinically, 18 of these patients were cured and 4 improved. It is therefore concluded that antigenic preparations exert a favourable effect on the enzymatic activity of the large intestine in chronic dysentery.

S. W. Waydenfeld

Cardiovascular System

735. **Restrictive Heart Disease: Diagnosis and Treatment**
N. E. REICH. *Angiology* [*Angiology*] **11**, 387–397, Oct., 1960. 6 figs., 12 refs.

According to the author of this paper from the Jewish Chronic Disease Hospital, New York, a diagnosis of restrictive heart disease is based on the presence of dyspnoea, signs of increased venous pressure, loss of apex beat, alteration of the normal precordial thrust, and paradoxical pulse. Radiological signs include enlargement of the cardiac contour by pericardial effusion, altered pulsation of the heart wall on fluoroscopy, and radiological evidence of calcification. Electrocardiography usually shows inversion of the T wave, low voltage, and various disturbances of conduction. The causes of restrictive heart disease are pericardial effusion due to infection, infarction, collagen disease, or malignancy; constrictive pericarditis, which is usually tuberculous in origin; myocardial disease, such as amyloid disease; and endocardial disease, such as endocardial fibroelastosis. Treatment in the case of constrictive pericarditis is surgical, otherwise symptomatic treatment and treatment of the primary condition if diagnosed form the basis for success. *J. Robertson Sinton*

736. **Experience with Perfusion Hypothermia Using an Improved Rotating Disc Oxygenator**
F. GERBODE, J. J. OSBORN, and J. B. JOHNSTON. *Thorax* [*Thorax*] **15**, 185–192, Sept., 1960. 8 figs., 15 refs.

An improvement in the immediate results of intracardiac surgery at the Presbyterian Medical Center, San Francisco, has been achieved by employing a combination of hypothermia and perfusion. In this paper the authors discuss the merits of using a variable degree of hypothermia in conjunction with a pump-oxygenator such as a modified Melrose oxygenator, the larger disks of which allow of a smaller priming volume. They consider that such a combination gives a greater safety margin and, since it allows a smaller minute volume of perfusion, diminishes the amount of blood which passes through the coronary sucker and thus lessens the risk of haemolysis. In their experience the more complex the cardiac condition under treatment, the lower the temperature should be reduced.

They have also found that the rate of elimination of carbon dioxide diminishes rapidly as the patient is cooled, and therefore the pressure of CO_2 should be kept between 4% and 6% at all times if possible. However, the CO_2 content of the oxygenator must be reduced when rewarming is started so that the excess absorbed by the patient can be more readily excreted. Experience has shown that the serum potassium level follows the venous *p*H closely and may not return to normal until 2 days after the operation. Since the adoption of the method described the survival rate in all types of case treated by the authors has been improved and postoperative morbidity has been reduced. These conclusions are based on the results in 190 patients, in 59 of whom the temperature was reduced below 28° C. *J. R. Belcher*

737. **Pressure Curves in Obstruction to Left Ventricular Outflow (Excluding Aortic Valvular Stenosis).** (Les courbes de pression des obstacles à l'éjection du ventricule gauche (à l'exclusion des sténoses aortiques orificielles))
P. SOULIÉ, J. JOLY, J. CARLOTTI, and J. FORMAN. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **35**, 843–863, Aug. [received Oct.], 1960. 12 figs., 7 refs.

Improvements in the techniques of left heart catheterization and open heart surgery have revealed unexpected complexities in the nature of aortic stenosis. In this paper from the Hôpital Broussais, Paris, 7 cases are described, in 5 of which the obstruction was situated below the valve and in 2 above it, the valve itself being normal in all. In such cases precise diagnosis is possible only by obtaining accurate pressure measurements at catheterization. The authors' approach to the region of the aortic valve was either retrograde via the axillary or femoral artery and past the valve into the ventricle, or antegrade through the bronchoscope and left atrium into the ventricle.

In the 2 cases of supravalvular stenosis determination of the pressure curves between the valve and the stenosis showed the expected pattern, that is, a high systolic pressure equalling that in the ventricle and a diastolic pressure equalling that in the aorta. In 4 of the 5 cases of infravalvular stenosis the pressure curves typical of an infundibular chamber were found just below the valve—that is, a systolic pressure equalling that in the aorta and a diastolic pressure identical with that in the ventricle. The 5th case was not, at catheterization, distinguishable from valvular stenosis, but at operation and necropsy there was found an extremely narrow passage immediately below the valve which was due to extreme muscular hypertrophy and superimposed endocardial fibrosis. *J. A. Cosh*

738. **An Aid to Identification of the Murmur of Aortic Stenosis with Atypical Localization**
R. P. HENKE, H. W. MARCH, and H. N. HULTGREN. *American Heart Journal* [*Amer. Heart J.*] **60**, 354–363, Sept., 1960. 9 figs., 12 refs.

Difficulty in the diagnosis of aortic stenosis may arise when the murmur is loud, or in some cases exclusively heard, at the apex and faint at the base of the heart, suggesting an origin in the mitral valve. The phonocardiographic studies here reported have confirmed that in these circumstances the graphic form of the murmur remains diamond-shaped. Furthermore, in all

of 6 patients who had aortic stenosis and auricular fibrillation it was found that the intensity of the murmur varied directly with the length of the preceding diastole. The murmur of mitral insufficiency shows no such change. It is suggested that this variation in intensity of the murmur with cycle length may be of value diagnostically and may be detected clinically. *C. Bruce Perry*

739. **The Use of Direct Stimulating Myocardial Electrodes in Complete Atrioventricular Block**
B. S. Levowitz, W. B. Ford, and J. W. Smith Jr. *Journal of Thoracic and Cardiovascular Surgery* [*J. thorac. cardiovasc. Surg.*] **40**, 283–297, Sept., 1960. 6 figs., 16 refs.

This paper from the University of Pittsburgh, Pennsylvania, describes 3 cases of complete atrioventricular block due to atherosclerotic heart disease treated by the insertion of electrodes from an external pacemaker direct into the ventricular myocardium. By this means a heart rate of 60 to 70 beats per minute can be maintained in patients whose rate would otherwise remain at 20 to 40 per minute and be accompanied by frequent Stokes–Adams attacks. The current used was initially 2 to 3 mA., gradually increased over 3 to 8 weeks, the appearance of frequent dropped beats signalling the need for higher current. Thereafter current requirements generally remained constant at 5 to 15 mA. The apparatus was transistorized, working off a 9-volt battery and supplying about 50 volts, the stimulus being approximately 2 msec. in duration. The first 2 cases described were treated initially by means of electrodes applied externally, but this method requires a high initial and a steadily increasing voltage as the resistance of the skin and chest wall seems to increase. A photograph showing the pigmentation and skin ulceration which this method produces is included.

A serious drawback to the insertion of electrodes into the heart is an almost inevitable sepsis passing down the track of the wire through the chest wall and leading eventually to sepsis at the site of insertion into the ventricle. [It is clear that more recent methods in which the stimulating current is induced through the chest wall without the need for a transthoracic cable are a great advance.] The authors suggest that a pacemaker is indicated when Stokes–Adams attacks are frequent, there is progressive ventricular slowing and poor output, and the ventricular rate is less than 20 per minute.
G. S. Crockett

740. **A Myocardial Syndrome. With Particular Reference to the Occurrence of Sudden Death and of Premature Systoles Interrupting Antecedent T Waves**
F. H. Smirk and D. G. Palmer. *American Journal of Cardiology* [*Amer. J. Cardiol.*] **6**, 620–629, Sept., 1960. 3 figs., 41 refs.

This paper from the University of Otago, New Zealand, describes a syndrome of which the chief electrocardiographic sign is interruption of the T wave by a succeeding premature QRS complex. The authors have studied 80 patients showing this type of abnormality and in addition have examined many published electrocardiograms for T-wave interruption. Features of the syndrome include myocardial damage and sudden death, multiple premature ventricular complexes, aberration in the form of ventricular complexes of supraventricular origin, and variation in the interval between successive ectopic beats and the preceding sinus complexes. Changes in the T-wave immediately following these ectopic beats are sometimes observed.

Clinically, this R-on-T-wave phenomenon is usually associated with significant heart disease, such as acute or chronic myocardial ischaemia, hypertensive heart disease, and such cardiomyopathies as Fiedler's and Chagas's myocarditis and influenzal myocardial endocarditis. T-wave interruption during the acute stage of myocardial infarction indicates an added danger to the patient. Sudden death may occur, possibly indicating vulnerability to ventricular fibrillation. There is a variable period in late systole during which an electric shock may precipitate ventricular fibrillation, and it is suggested that the ectopic beat occurring at this precise period may occasionally have the same effect. As the syndrome is frequently associated with sudden death the prophylactic administration of quinidine is recommended as soon as the phenomenon is recognized. *T. Semple*

741. **Clinical Assessment of Mitral Orifice in Patients with Regurgitation**
P. G. F. Nixon and G. H. Wooler. *British Medical Journal* [*Brit. med. J.*] **2**, 1122–1123, Oct. 15, 1960. 2 figs., 11 refs.

An investigation of 20 patients suffering from mitral regurgitation at the General Infirmary at Leeds suggested that the size of the mitral orifice may be predicted with reasonable accuracy from the cardiac impulse and heart sounds. The size of the orifice so estimated was confirmed at operation in all cases.

In cases where the mitral orifice was less than 1·5 cm. in diameter the mitral diastolic murmur began quietly, the third heart sound was absent, and there was not a late diastolic rise in left atrial pressure. With an orifice measuring 2 cm. or more the left ventricle was invariably palpable, the diastolic murmur had an explosive onset, the third heart sound was present in most cycles, and there was a rise of left atrial pressure in diastasis. It is suggested that the quietly beginning murmur be called the "low-flow" mitral diastolic murmur, and the loud murmur the "high-flow" mitral diastolic murmur.
R. L. Hurt

742. **Association of "Silent" Mitral Stenosis with Massive Thrombi in the Left Atrium**
B. Surawicz and M. A. Nierenberg. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 423–431, Sept. 1, 1960. 10 figs., 34 refs.

The authors present, from the University of Vermont College of Medicine, Burlington, the cases of 4 patients in whom mitral stenosis coexisted with massive thrombosis of the left atrium. In describing the clinical features of each of these cases they note particularly that a diastolic murmur could not be heard or demonstrated by phonocardiography in any of them, despite the fact that

such a murmur had previously been present. Chest pain was a symptom in 2 cases, but it was attributed to pleurisy accompanying pneumonia. An elevated third segment along the left cardiac border, which may often be seen radiographically in the presence of mural thrombosis of the left atrium, was not observed in any of these cases.

The correct diagnosis was made clinically in one case, at operation in another, and at necropsy in the remaining 2. The authors conclude that massive thrombosis of the left atrium may be one of the factors contributing to the disappearance of typical auscultatory findings in patients with mitral stenosis.

A. J. Karlish

CORONARY DISEASE AND MYOCARDIAL INFARCTION

743. Nicotinic Acid in the Treatment of Ischaemic Heart-disease

C. E. GOLDSBOROUGH. *Lancet* [*Lancet*] **2**, 675–677, Sept. 24, 1960. 13 refs.

In a general practice the author has treated 60 patients with ischaemic heart disease with nicotinic acid (and in some cases nicotinamide) since 1946; 24 had cardiac infarction and 36 suffered from angina of effort. Electrocardiography was usually carried out only in the later stages of the illness, the original diagnosis being made in nearly every case on clinical grounds only.

Coronary thrombosis was treated immediately with nicotinic acid, 50 mg. being injected hypodermically and 100 mg. administered under the tongue at the same time. In 18 cases immediate relief was experienced as soon as the usual flushing occurred, but often further injections of nicotinic acid were needed to maintain the relief. Only in 2 cases did flushing and relief of pain fail to follow the injections, and only these 2 patients were sent to hospital. In the remainder further treatment consisted in the oral administration of 100 mg. of nicotinic acid 3 times daily.

In cases of angina of effort up to 200 mg. of nicotinic acid was given by mouth 3 times a day immediately after food. In both types of case it was found that a smoother and more sustained vasodilatation was obtained by giving nicotinamide before the meal in addition to the nicotinic acid. The usual maintenance dose was 50 mg. of each thrice daily, this being occasionally increased up to 200 mg. After 2 or 3 years of continuous treatment many patients were able to return to their former occupation.

The author attributes the effect of this treatment to the vasodilatation and reduction in plasma cholesterol level produced by nicotinic acid and nicotinamide.

[This uniformly favourable experience of the author with nicotinic acid in the treatment of coronary arterial disease is at variance with the clinical experience (published and unpublished) of others, and these claims should be reinvestigated. Nicotinic acid in daily doses of 3 g. or more reduces the plasma cholesterol level permanently, but smaller doses have no such effect, nor does nicotinamide in any dosage reduce the plasma cholesterol level (Parsons *et al.*, *J. Amer. med. Ass.*, 1957, **165**, 234). No proof of an anti-atherogenic effect of nicotinic acid has yet been presented.]

Z. A. Leitner

744. A Trial of a New Monoamine Oxidase Inhibitor in Angina Pectoris

D. PHEAR and W. C. WALKER. *British Medical Journal* [*Brit. med. J.*] **2**, 995–996, Oct. 1, 1960. 8 refs.

This paper from the Central Middlesex Hospital, London, reports a trial of the drug 1-pivaloyl-2-benzylhydrazine (" tersavid ") in the treatment of 20 patients with typically severe angina, constant in degree. A double-blind cross-over technique was used in which each patient acted as his own control, taking tersavid and inert tablets for periods of one month each. Only one patient appeared to benefit from the drug in a dosage of 250 mg. daily.

Negative results were also obtained in a similar trial of pentaerythritol tetranitrate in high dosage (60 mg. thrice daily).

T. Semple

745. Isoenzymes and Myocardial Infarction

F. WRÓBLEWSKI, C. ROSS, and K. GREGORY. *New England Journal of Medicine* [*New Engl. J. Med.*] **263**, 531–536, Sept. 15, 1960. 11 figs., 3 refs.

By means of starch-gel electrophoresis, human plasma lactic dehydrogenase (pLD) activity has been shown to consist of five isoenzymes designated pLD_1, pLD_2, pLD_3, pLD_4 and pLD_5. Plasma from normal adults has a typical isoenzyme pattern in which $pLD_2 < pLD_1 < pLD_3 < pLD_5 < pLD_4$. Human tissues contain one or more of these isoenzymes, and each tissue has an individual and characteristic isoenzyme pattern. Cardiac muscle contains LD_4 and LD_5, with a preponderance of LD_5. No other human tissue studied has the same isoenzyme composition as heart tissue.

Transmural and subendocardial myocardial infarction causes an alteration in the isoenzyme pattern of plasma resulting in an increase in pLD_4 and pLD_5, and characteristically pLD_5 is greater than pLD_4. The plasma isoenzyme pattern seen in the course of myocardial infarction appears to be a more sensitive, specific and lasting parameter of myocardial necrosis than the measurement of total serum or plasma enzyme activity.

Diseases of organs other than the heart cause changes in the plasma isoenzyme pattern, but these alterations are different from those observed after myocardial infarction. The plasma isoenzyme patterns seen in diseases of other organs will be reported subsequently.—[Authors' summary.]

746. The Low Incidence of Myocardial Infarction in Patients with Portal Cirrhosis of the Liver: a Review of 639 Cases of Cirrhosis of the Liver from 17,731 Autopsies

W. L. HOWELL and W. C. MANION. *American Heart Journal* [*Amer. Heart J.*] **60**, 341–344, Sept., 1960. 25 refs.

It has frequently been stated that in chronic alcoholics and patients with portal cirrhosis the incidence of atherosclerosis is lower than in the general population. In an attempt to confirm this the authors have analysed, at the

Armed Forces Institute of Pathology (Georgetown University Medical School), Washington, D.C., the records of 17,731 patients coming to necropsy. Of 639 of these in whom there was a confirmed diagnosis of portal cirrhosis, Laënnec's cirrhosis, or post-necrotic cirrhosis of the liver, 32 were found to have myocardial infarcts, an incidence of 4·9%. In a random 5% sample of the remaining, non-cirrhotic, subjects the incidence of myocardial infarction was 20·2%. Thus in the groups studied myocardial infarction was less than one-fourth as common in patients with hepatic cirrhosis as in non-cirrhotic patients. The incidence of recent myocardial infarction was 1·8% among patients with cirrhosis and 10% in the others, this trend being evident even in the presence of diabetes mellitus. It has been noted by other workers that clot lysis (fibrinolysis) is both active and prolonged in patients with cirrhosis of the liver. The possible relationship between this and the low incidence of myocardial infarction is discussed.

C. Bruce Perry

BLOOD VESSELS

747. **Serum Transaminase Activity in Dissecting Aneurysm of the Aorta**

P. Adams and E. M. Jacoby. *British Medical Journal* [*Brit. med. J.*] **2**, 1131–1132, Oct. 15, 1960. 10 refs.

Serial estimations of serum glutamic–oxalacetic transaminase and serum glutamic–pyruvic transaminase levels were made in 3 cases of dissecting aneurysm of the aorta at the Royal Infirmary, Cardiff, in an effort to determine whether these readings would assist in making the diagnosis. Factors which may give rise to increased transaminase values are myocardial necrosis due to subepicardial haemorrhage, acute liver congestion, codeine therapy, and renal failure. Therefore if all these can be excluded, a normal transaminase reading would be in favour of a diagnosis of dissecting aneurysm of the aorta and not one of coronary thrombosis. *J. B. Wilson*

748. **Atherosclerosis and beta-Glucuronidase**

S. Kayahan. *Lancet* [*Lancet*] **2**, 667–669, Sept. 24, 1960. 9 refs.

Thyroid extract, oestrogenic hormones, and heparin, which all lower the high plasma cholesterol level associated with atherosclerosis, are also known to increase the serum β-glucuronidase activity. For this reason the role of β-glucuronidase in the pathogenesis of atherosclerosis was investigated at the University of Istanbul.

Forty 2-week-old chickens were divided into 4 equal groups, one of which was fed on commercial chicken mash, while the other 3 were fed on the same mash to which 2% of cholesterol and 5% of cotton-seed oil had been added. In addition the chickens in Group 3 were given 500 units of β-glucuronidase daily by injection over the whole period of the experiment and those in Group 4 were given 800 units daily by injection after the first 6 weeks. After 10 weeks the animals were killed, the aorta examined for atherosclerosis, and the serum β-glucuronidase activity and total lipid and cholesterol levels estimated. No atherosclerosis was found in Group 1, severe atherosclerosis was found in Group 2, and moderate atherosclerosis was found in Groups 3 and 4. The serum cholesterol level was high in Group 2, but was only moderately raised in Groups 3 and 4, in which an increase in the serum β-glucuronidase activity was also found. These findings, in the author's opinion, "suggest that β-glucuronidase has a preventive and probably therapeutic effect on experimental atherosclerosis".

Investigations were then carried out on human subjects with and without atherosclerosis. The average β-glucuronidase activity in the serum of 20 normal patients was considerably higher than in that of 20 atherosclerotic patients, and a similar difference was found between the average β-glucuronidase activity in the aortic intima of 10 normal subjects and that of 10 patients with atherosclerosis. Ten patients suffering from coronary arterial disease were given 25,000 units of β-glucuronidase by intramuscular injection daily for 4 weeks. The serum total lipid and cholesterol levels, the serum $\beta:\alpha$ lipoprotein ratio, and the coagulability of the blood were significantly reduced in all cases by the end of this period.

These results suggest that β-glucuronidase has an effect on the metabolism of lipids and also of proteins. Thus a defect in the enzyme "may play a part in the pathogenesis of atherosclerosis, and β-glucuronidase may have a therapeutic effect". *Z. A. Leitner*

749. **Tolbutamide in the Treatment of Thromboangiitis Obliterans**

I. Singh and N. S. Brara. *Lancet* [*Lancet*] **2**, 625–626, Sept. 17, 1960. 3 refs.

The finding that tolbutamide relieved anginal pain (*Lancet*, 1959, **2**, 1141) led the authors to try this drug in thromboangiitis obliterans, and they now report their results in 36 cases of this disease in Indian men. The patients' ages ranged from 25 to 42 years, and in 13 cases one or more limbs had already been amputated on account of the disease. All previous treatment was discontinued and tolbutamide, 0·5 g., was given with the three main meals. Treatment was stopped when symptoms ceased and the duration of relief assessed. All the patients noticed improvement within 2 to 5 days of starting treatment and were symptom-free before the end of the 4th week. Agonizing pain at rest was relieved even more strikingly than when repeated doses of morphine were given, although in 2 cases the paroxysmal lancinating pain of neurotic origin did not respond. When tolbutamide therapy was discontinued relief persisted for one to 7 weeks, and maintenance therapy in 3 cases has controlled symptoms for over 2 years.

G. S. Crockett

750. **The Significance and Classification of Fat-embolism**

S. Sevitt. *Lancet* [*Lancet*] **2**, 825–828, Oct. 15, 1960. 3 figs., 21 refs.

From the Birmingham Accident Hospital the author reports a study of pulmonary and systemic fat embolism based upon the findings in 100 patients who died after

injury and came to necropsy and in 17 patients in whom the condition was diagnosed clinically. Pulmonary fat embolism was found at necropsy in 89 of the 100 cases examined post mortem, but was not associated with respiratory symptoms and had not been suspected during life. The author considers that pulmonary fat embolism does not cause significant symptoms or produce serious lung changes in previously healthy subjects, and that it is not responsible for death. Of the 100 patients, 24 had systemic emboli, all of these having pulmonary emboli as well. Only 7 patients had had cerebral symptoms consistent with fat embolism during life.

The author divides the cases of systemic embolism into the following categories. (I) Fulminating cases, in which death occurs one to 3 days after severe injury, usually with multiple fractures, death being usually preceded by paralytic symptoms, stupor, and coma. (II) Cases showing the classic syndrome, in which cerebral and neurological symptoms such as restlessness, confusion, coma, paralyses, and incontinence develop within 24 to 48 hours of injury. These signs are accompanied by acute pyrexia, tachycardia, and respiratory distress, and on the 2nd or 3rd day by a characteristic petechial eruption on the neck, shoulders, and chest of much diagnostic importance. (III) Cases showing the incomplete syndrome; these can be subdivided into (1) those without respiratory symptoms; (2) those without cerebral symptoms; and (3) those without significant cerebral or respiratory symptoms. Cases illustrative of these various types are described. In the absence of the characteristic rash diagnosis is very difficult, and many undiagnosed cases are thought to survive with or without cerebral effects of the embolism. Tests for fat in the sputum, urine, and plasma are unhelpful, but needle biopsy of the kidney has been found of value in obscure cases, the finding of globules in the glomeruli being proof of systemic embolism and, by inference, of cerebral embolism. The mortality is high in patients in coma, but it seems that some patients can tolerate a certain amount of embolic fat in the brain without developing significant symptoms. *Bernard Isaacs*

SYSTEMIC CIRCULATORY DISORDERS

751. **Blood Pressure Lability: a Correlative Study**
A. M. Ostfeld and B. Z. Lebovits. *Journal of Chronic Diseases* [*J. chron. Dis.*] **12**, 428–439, Oct., 1960. 2 figs., 24 refs.

It is known that in both hypertensive and normotensive subjects there is a wide range in magnitude of both systolic and diastolic arterial blood pressure variability, and the authors have observed that those with greatest variability tend to exhibit hysterical, hypochondriacal, or anxious behaviour. They have now carefully investigated this in 17 patients with essential hypertension and 17 matched controls, relating the standard deviations of 7 systolic and 7 diastolic readings in both groups to personality assessments by the Minnesota Multiphasic Personality Inventory (M.M.P.I.). In both groups there was a significant positive correlation between systolic and diastolic lability and the scores on the hysteria, hypochondriasis, and psychopathic deviate scales of the M.M.P.I.—that is to say, there is a correlation between blood-pressure lability and impulsive, hypochondriacal, and hysterical behaviour. The hope is expressed that this study may help towards the eventual delineation of a subgroup of the larger hypertensive population that is characterized by labile hypertension and certain neurotic behaviour traits. It is suggested that in such patients the hypertensive disease might be mitigated by a good physician–patient relationship and the adoption of new, more favourable, attitudes. *K. G. Lowe*

752. **Blood-volume and Tolerance to Pentolinium in the Treatment of Hypertension**
V. Rønnov-Jessen. *Lancet* [*Lancet*] **2**, 669–671, Sept. 24, 1960. 15 refs.

At the Copenhagen County Hospital, Gentofte, the mechanism of the development of tolerance to pentolinium ("ansolysen") was studied in 8 ambulant patients with severe constant hypertension. Sensitivity to the drug was expressed as the greatest fall in mean blood pressure in the erect posture which followed the intravenous injection of a fixed dose (ranging from 1 to 3·5 mg. in different patients) of pentolinium bitartrate. The blood volume, determined by the radioactive chromium method, and the pentolinium sensitivity were measured at various times before and during treatment.

In 6 of the 8 patients the blood volume increased during treatment and concurrently the sensitivity to pentolinium decreased; in the other 2 patients the blood volume decreased and at the same time sensitivity to pentolinium became greater. After combined treatment of 6 patients with pentolinium and chlorothiazide or hydrochlorothiazide the blood volume decreased in 5 and the sensitivity to pentolinium simultaneously increased. In 2 patients so treated restoration of the blood volume to the previous level by the infusion of salt-free dextran resulted in a restoration of pentolinium sensitivity to its original value. In explanation of these facts the author suggests that as a consequence of the fall in blood pressure following pentolinium therapy the blood volume increases; when this occurs the neurogenic component of blood-pressure regulation diminishes and consequently the effect of pentolinium also decreases.

Bernard Isaacs

753. **Sympathetic Blockade in Treatment of Hypertension: Clinical Trial of Bretylium Tosylate**
C. P. Lowther and R. W. D. Turner. *British Medical Journal* [*Brit. med. J.*] **2**, 1049–1053, Oct. 8, 1960. 1 fig., 15 refs.

Writing from the Western General Hospital, Edinburgh, the authors report on the use of sympathetic blockade with bretylium tosylate in the treatment of 43 patients with hypertension, all but 3 of whom had a diastolic blood pressure greater than 110 mm. Hg. In addition to the high diastolic blood pressure there were objective signs of secondary changes in the heart, kidneys, or optic fundi. Impaired renal function was defined as a phenolsulphonephthalein excretion below

20% in 15 minutes or an endogenous creatinine clearance below 100 litres in 24 hours, while renal failure was defined as a blood urea level greater than 40 mg. per 100 ml. The drug was initially given in a dosage of 100 mg. three times a day after meals, increases of 100 to 300 mg. a day being made at intervals of 2 to 3 days. The average daily dose was 200 mg., but wide variations in sensitivity to the drug were encountered; thus in one case syncope due to postural hypotension occurred with a daily dose of only 300 mg., whereas in another the blood pressure was resistant to 6,000 mg. a day. The results were assessed as " good " if the blood pressure was reduced by 20 to 30 mm. and the diastolic pressure to below 100 mm. Hg and as " fair " when the reduction in blood pressure was 20 to 30 mm. and the diastolic pressure fell to between 100 and 110 mm. Hg. If there was no significant fall in the blood pressure the result was graded as " poor ".

On this basis, after an average period of 6 months results could be graded as good in 8 patients (19%), fair in 8 (19%), and poor in the remaining 27 (62%). Even by the criteria of Dollery *et al.*, working at Hammersmith Hospital, London, (*Lancet*, 1960, **1**, 296; *Abstr. Wld Med.*, 1960, **28**, 209) only 38% of the results would have been good. The authors comment that by either standard the results are far from satisfactory, and as a result of the drug's poor hypotensive action, the development of tolerance, and the appearance of a new group of side-effects treatment with bretylium tosylate has been abandoned in 35 (81%) of the patients. Tolerance to the drug was such that 32 (74%) of the patients required a steady increase in dosage and thus had to be under close and constant supervision. This caused anxiety which, with the addition of unpleasant side-effects, sometimes made it difficult to induce patients to attend for follow-up. The authors suggest that the wide variation in response to the drug is probably due to variation in degree of absorption from the intestine, with the result that the blood pressure fluctuates considerably over relatively short periods of time. In this connexion they emphasize the uselessness of isolated blood pressure readings in such cases. One of the major disadvantages of the drug was its tendency to cause syncope, which they found more troublesome than with any other hypotensive agent. Several case histories are presented to illustrate the dangers of this complication. In no patient who suffered syncope was the standing diastolic pressure below 150 mm. Hg when last recorded. Other side-effects occurred in 39 of the 43 patients, but in most cases could have been tolerated had the drug been effective as a hypotensive agent. Although many of them tended to diminish as treatment progressed, some became worse, notably pain over the parotid gland, which occurred in 40% of the cases. The remaining side-effects included dizziness, a feeling of constriction in the chest (15 cases), dyspnoea, diarrhoea, headache, muscular weakness, mental changes, nasal congestion, and sexual difficulties.

In view of these drawbacks the authors turned to guanethidine and report briefly their experience with this drug, which they consider to be superior to bretylium in that its side-effects are less troublesome and fewer patients develop tolerance. They conclude that while bretylium tosylate marks a great advance pharmacologically and physiologically in having a selective action on the sympathetic division of the autonomic nervous system, clinically it has proved disappointing. In their opinion it is not a practicable or effective form of treatment of hypertension and may in fact be dangerous.

J. Warwick Buckler

754. **Five-year Survival of Patients with Malignant Hypertension Treated with Antihypertensive Agents**

E. R. MOHLER JR. and E. D. FREIS. *American Heart Journal* [*Amer. Heart J.*] **60**, 329–335, Sept., 1960. 3 figs., 21 refs.

In untreated cases of malignant hypertension (defined as those with papilloedema) the mortality has been variously reported as between 79% and 90% within a year, while the 5-year survival in drug-treated cases has been stated to range from 33% to 50%. The present authors have reviewed the case histories of 64 patients treated with antihypertensive drugs at Mt. Alto Veterans Administration and Georgetown University Hospitals, Washington, D.C., between 1949 and 1953 and followed up to the end of 1958 with a view to determining the effects of treatment on the course of the disease. There were 41 Caucasian and 23 negro patients with an age range of 23 to 61 years (mean 45·7 years). The drugs used were derivatives of rauwolfia, hydrallazine, veratrum and its derivatives, hexamethonium, pentolinium, and chlorothiazide; a few patients also received chlorpromazine, phenobarbitone, or meprobamate.

The average blood-pressure level before treatment was instituted was 221/141 mm. Hg, and the last available mean blood pressure was 192/119 mm. Hg. The average reduction in blood pressure was significantly greater in those surviving 5 years or longer. Absence of renal damage was also found to be an important factor in 5-year survival. At the end of the period of observation 14 of the 64 patients still survived, the commonest cause of death in the remainder being cerebrovascular accident. This is in contrast to the finding of other authors that renal failure is the most frequent cause of death in untreated cases of malignant hypertension. In cases in the present series examined at necropsy marked cerebral atheroma with involvement of the aorta and coronary arteries was a consistent feature and the average weight of the heart was just over twice normal.

The authors were surprised to find that negroes survived as long as Caucasians, and they discuss the special reasons for this finding.

G. S. Crockett

755. **Hyperuricaemia Related to Treatment of Hypertension**

C. T. DOLLERY, H. DUNCAN, and B. SCHUMER. *British Medical Journal* [*Brit. med. J.*] **2**, 832–835, Sept. 17, 1960. 3 figs., 7 refs.

Gout and familial hyperuricaemia are known to be associated with hypertension and renal disease, and this has prompted the authors to study the serum uric acid levels of patients attending the hypertension clinic of the Hammersmith Hospital, London. The survey covered

157 patients attending during a 6-month period, of whom 103 were receiving treatment with ganglion-blocking drugs, reserpine, and chlorothiazide, alone or in combination, the others having no drug therapy. The age and sex distribution in the treated and untreated groups were similar, but the severity of the hypertension was not; thus 22 patients in the treated group had malignant hypertension compared with 6 in the untreated group.

The serum uric acid level was more often raised in the treated group, 32 (30%) of whom had a value above 7 mg. per 100 ml., compared with only 2 (4%) of the untreated patients. In contrast, the mean blood urea level of the treated group was only slightly above that of the untreated group. In 16 cases the blood uric acid level was estimated during treatment and also during periods when the drug was withdrawn for any reason, such as intercurrent illness or intolerance. In 14 of these cases there was a rise in the uric acid level when the drug was given and a fall when it was withdrawn, the greatest increase taking place after the administration of chlorothiazide.

It is concluded that the serum uric acid level is often raised in hypertension and that treatment, especially with chlorothiazide, is largely responsible for this.

David Phear

756. **Effect of Prolonged Treatment with Hypotensive Drugs on Renal Function in Hypertension**

J. MACKINNON and J. D. S. HAMMOND. *British Medical Journal* [*Brit. med. J.*] **2**, 987–990, Oct. 1, 1960. 4 figs., 12 refs.

The authors of this paper from the Universities of Manchester and Sheffield have used serial estimations of the glomerular filtration rate (inulin clearance), effective renal plasma flow (*p*-aminohippurate clearance), and blood urea level to assess the effects of prolonged treatment with ganglion-blocking drugs combined with hydrallazine, chlorothiazide, rauwolfia, or veratrum in 8 cases of malignant and 7 of severe benign hypertension. Four patients with malignant hypertension had azotaemia before treatment was started; their clearance values were low and all died within 10 months. The 2 who survived the longest lost their severe symptoms; their blood urea level rose transiently in the first week of treatment and then, despite a fall in blood pressure, remained at the pre-treatment level until shortly before death, when it rose suddenly. Of the 4 patients with malignant hypertension whose blood urea level was initially normal, one died of renal failure, in 2 the renal clearance values deteriorated, and the other, who had chronic glomerulonephritis, showed no change during 5 years' observation. Of the 7 patients with benign hypertension, 5 were treated for 5 years or longer; in 2 there was no change and in 3 there was deterioration in the renal clearance values. The other 2 were observed for shorter periods; they showed no change in renal plasma flow, but one showed an improvement in glomerular filtration rate.

The authors consider that prolonged treatment with hypotensive drugs does not impair the renal circulation in hypertensive subjects with good renal function, since in their patients a fall in renal blood flow occurred only after several months of treatment and was most probably due to the natural progress of the disease. This was possibly related to failure of the treatment to maintain the blood pressure within normal limits throughout the 24 hours.

K. G. Lowe

757. **A Screening Test for Adrenal or Unilateral Renal Forms of Hypertension Based upon Postural Change in Blood Pressure**

D. KINSEY, G. P. WHITELAW, and R. H. SMITHWICK. *Angiology* [*Angiology*] **11**, 336–342, Aug. [received Oct.], 1960. 8 figs., 3 refs.

The effects of postural change on blood pressure were observed in 37 patients with humoral hypertension (phaeochromocytoma in 18, adrenal cortical hyperfunction in 8, and unilateral renal disease in 11) and compared with those in 100 consecutive hypertensive patients who subsequently underwent lumbodorsal sympathectomy; most, if not all, of these 100 patients probably had essential hypertension. Blood pressure was recorded at 1-minute intervals with the patient recumbent for 5 minutes and then standing for 5 minutes. There were 9 possible responses, depending upon whether the systolic and diastolic pressures rose, fell, or remained unchanged when the upright position was assumed. On standing, 26 of the 100 patients with presumed essential hypertension and 30 of the 37 patients with adrenal or unilateral renal hypertension showed a fall in both systolic and diastolic pressures, a fall in systolic pressure with no change in diastolic pressure, or a fall in systolic and a rise in diastolic pressure of less than 11 mm. Hg. It is pointed out that many of the special procedures for the detection of "curable" hypertension, such as the Howard test, catechol amine and corticoid excretion studies, and aortography, are time-consuming and tedious. The postural change in blood pressure, as here determined, could possibly be used as a rough screening test in the selection of hypertensive patients.

K. G. Lowe

758. **Clinical and Statistical Evaluation of the Results Obtained by Sympathectomy in 285 Cases of Various Peripheral Vascular Diseases**

S. BOGUSLAWSKI, S. BANACH, and M. DABROWSKI. *Journal of Neurosurgery* [*J. Neurosurg.*] **17**, 824–829, Sept., 1960.

In this paper from the Department of Neurosurgery, Medical Academy, Warsaw, the authors report the results of sympathectomy in the treatment of peripheral vascular disease during the period 1936–57. The largest group of patients consisted of 191 with Buerger's disease, of whom 82 were followed up for periods of 2 to 10 years after operation. Of these, great improvement was maintained in 37·8%, slight or moderate improvement in a further 41·5%, while 20·7% derived no benefit from the procedure. As might have been expected the best results were obtained in the milder cases, 4 out of 8 patients with fulminating disease showing no improvement. The authors comment on the observation that the late results showed a higher percentage of great improvement than the earlier ones, a phenomenon which they term "polar-

ization" of results [but which they do not attempt to explain].

In 66 cases of arteriosclerosis the results were much less good, great improvement being recorded in only 3% of cases, with moderate improvement in a further 56·1%. The "polarization" effect was again evident. Of 17 patients with Raynaud's disease, 8 were observed for more than 2 years, and in these the long-term results were less good than had been hoped from the immediate results, one patient showing no sustained improvement, 3 only slight improvement, and 2 moderate and 2 great improvement. [In view of the small number in this group it is doubtful whether these results are generally applicable.]

Of the patients with Buerger's disease, 46 had eventually to undergo amputation, and the authors maintain that the previously performed sympathectomy enabled the level of amputation to be lowered and, in addition, facilitated healing of the stump. In 20 cases amputation of the foot or one or more toes only was necessary, while in 9 amputation below the knee and in 17 above it had to be performed. Of the 66 cases of arteriosclerosis, 19 came to amputation, which in 9 could be restricted to the foot or toes. Sympathectomy consisted in the majority of cases in the division of the pre-ganglionic fibres, and the bilateral operation is considered preferable even in cases in which the circulatory disturbance is confined to one side. The total mortality was 1·4%, and serious side-effects were not encountered in any of the survivors.

[In view of their strong advocacy of sympathectomy for peripheral vascular disease, especially the more severe cases, it is to be regretted that a comparable series treated conservatively was not available to the authors so as to allow of a more convincing statistical analysis than is presented in this paper.] *H. F. Reichenfeld*

PULMONARY CIRCULATION

759. **The Pulmonary Circulation in Pulmonary Oedema Complicating Left Heart Disorders in Man.** (La circulation pulmonaire au cours de l'œdème pulmonaire compliquant les cardiopathies gauches chez l'homme)
J. Lenègre, L. Scebat, and J. Renais. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **35**, 864–877, Aug. [received Oct.], 1960. 1 fig., 10 refs.

Pulmonary oedema occasionally develops during the course of cardiac catheterization of the right heart, usually being precipitated by the supine posture, the performance of an exercise test, or anxiety in a patient whose pulmonary capillary pressure is already high. Although such a development calls for fairly urgent corrective measures, such as sitting the patient upright, administering morphine and oxygen, or withdrawing blood, there is in some cases enough time to carry out some haemodynamic measurements during the acute phase.

In the course of 2,260 right-heart catheterizations performed at the Hôpital Boucicaut, Paris, pulmonary oedema developed 50 times, being confined to the group of patients (1,075) with left-sided, mainly rheumatic, heart disease; adequate measurements were possible in 39 of the 50. All but one had a pulmonary capillary pressure over 32 mm. Hg, the one exception being a patient with a recent pulmonary embolus in whom this pressure was 20 mm. Hg. In all cases the pulmonary arterial pressure was raised, as was also the pressure gradient between the pulmonary artery and capillaries. Usually, but not in all cases, oxygen consumption and cardiac output increased, and there was a moderate rise in pulmonary arteriolar resistance. Very high resistances were not found, and probably protect against the development of pulmonary oedema. The detailed findings are presented in a table. In conclusion it is noted that some patients with equally high pulmonary capillary pressures did not develop oedema, indicating that other factors, such as tissue fluid tension and the degree of permeability of the alveolar lining, play a part in the development of pulmonary oedema. *J. A. Cosh*

760. **Structural Changes in the Intrapulmonary Vessels Associated with Alterations in the Pulmonary Circulation in Pneumosclerosis [Pulmonary Fibrosis].** (К вопросу о перестройке внутрилегочных сосудов в связи с изменением легочного кровообращения при пневмосклерозе)
A. V. Ryvkind. *Архив Патологии* [*Arh. Patol.*] **22**, 41–47, No. 5, 1960. 6 figs., 6 refs.

Histological examination of the pulmonary vasculature in specimens from cases [number unstated] of pulmonary fibrosis revealed the following changes. The inflammatory processes leading to fibrosis of the lung also cause atrophy of the pulmonary arterial circulation accompanied by compensatory hypertrophy of the bronchial arterial system. The bronchial arteries increase in diameter and also in length, resulting in tortuosity. Later, anastomoses are formed between the two arterial systems. A peculiar feature seen in the larger of these anastomoses is "penetration" of the bronchial artery into the lumen of the pulmonary artery, or rather there occurs, as it were, a plastic reconstruction of the latter so that a structure resembling the wall of the bronchial artery grows within the lumen of the pulmonary artery. *A. Swan*

761. **Pulmonary Embolism: a Study of Late Prognosis**
D. Phear. *Lancet* [*Lancet*] **2**, 832–835, Oct. 15, 1960. 4 figs., 17 refs.

The author reports that of 136 patients (mean age 63·6 years) diagnosed at the Central Middlesex Hospital, London, in the 3-year period 1957–9 as having had a pulmonary embolism, 71 survived. Of 68 of these who were followed up at an average of 17·6 months after the incident, 42 had recovered completely, 16 had mild or moderate dyspnoea, and 10 older patients, of average age 67, were severely disabled by cardiac failure. Of these 10 patients, 7 had clinically recurrent embolism and 3 of the 10 subsequently died. Two patients presented a clear picture of pulmonary hypertension and right ventricular failure, and the remainder had evidence of right ventricular hypertrophy. *Bernard Isaacs*

Clinical Haematology

762. **Successful Maintenance of Pernicious Anaemia Patients with Vitamin B_{12} and Intrinsic Factor for Long Periods**

L. ELLENBOGEN, W. L. WILLIAMS, and H. C. LICHTMAN. *British Medical Journal* [*Brit. med. J.*] **2**, 1066–1068, Oct. 8, 1960. 24 refs.

In a variable percentage of patients with pernicious anaemia oral preparations of vitamin B_{12} (cyanocobalamin) and hog intrinsic factor have failed to maintain satisfactory remission. In the present paper the results are reported of maintenance therapy with various commercial intrinsic-factor preparations of 24 patients with pernicious anaemia. The patients received daily either a capsule containing 50 mg. of hog intrinsic factor and 30 μg. of vitamin B_{12} or a similar capsule containing 60 mg. of hog intrinsic factor and 15 μg. of vitamin B_{12}. Of the 24 patients, 9 had previously been maintained (for 5 to 36 months) on other oral preparations. The ability of patients who were given a standard intrinsic-factor preparation to absorb vitamin B_{12} labelled with radioactive cobalt was determined quantitatively by measuring the level of radioactivity in the urine.

Only 2 patients showed any refractoriness to these oral preparations; one had required 20 times the usual amount of intrinsic factor for optimum absorption of vitamin B_{12} before any oral therapy, while one, after 22 months' treatment with other oral preparations and 7 and 17 months respectively with the two preparations studied, showed reduced absorption of vitamin B_{12}.

A. Ackroyd

763. **Clinical Analysis of 100 Cases of Severe Megaloblastic Anaemia of Pregnancy**

P. B. B. GATENBY and E. W. LILLIE. *British Medical Journal* [*Brit. med. J.*] **2**, 1111–1114, Oct. 15, 1960. 21 refs.

An analysis is presented of the clinical and obstetrical features of 100 cases of severe megaloblastic anaemia of pregnancy seen at the Rotunda Hospital, Dublin, over a 6-year period, representing an incidence of one case in 240 confinements. The lowest haemoglobin level was 2 to 2·9 g. per 100 ml. (one case) and the highest was 9·0 to 9·9 g. per 100 ml. (one case). Anaemia was not the presenting symptom in many cases, more prominent features being vomiting, diarrhoea, pyrexia, oedema, and albuminuria. The finding of megaloblasts in the bone marrow or in the buffy coat of the peripheral blood established the diagnosis. In some of the cases megaloblastic anaemia was a complication of carcinoma, Hodgkin's disease, lymphadenopathy, urinary infection, or epilepsy; it is suggested that administration of anticonvulsant drugs in epilepsy is a factor in the development of the anaemia. Generally, anaemia was diagnosed between the 31st and 40th weeks of gestation. The authors consider that oedema or albuminuria occurring without hypertension must be regarded as due to or associated with the anaemia, and not toxaemia. In their series there was a high incidence of prematurity (12·5% excluding multiple births), of hydramnios (9 cases), and of multiple pregnancy (8 cases); the neonatal death rate was high (6 cases), and could be explained by the frequency of premature labour, prematurity, and multiple pregnancy.

It is concluded that although no clear relationship between inadequate diet and the incidence of anaemia of pregnancy has yet been demonstrated in the British Isles, and the administration of supplementary folic acid may in a few cases mask severe underlying disease such as carcinoma or Addison's disease, routine antenatal administration of folic acid, at least in cases of multiple pregnancy, is advisable. *Ethel Browning*

764. **Prolonged Corticosteroid Therapy of Chronic Lymphocytic Leukaemia and the Closely Allied Malignant Lymphomas**

J. G. FREYMANN, J. B. VANDER, E. A. MARLER, and D. G. MEYER. *British Journal of Haematology* [*Brit. J. Haemat.*] **6**, 303–323, July [received Sept.], 1960. 6 figs., 43 refs.

The value of corticosteroid therapy in chronic lymphatic leukaemia with obvious secondary haemolytic anaemia is well recognized. Even if the classic manifestations of haemolysis are lacking it is generally assumed that anaemic patients with chronic lymphatic leukaemia giving a positive reaction to the Coombs test also have an occult haemolytic anaemia.

The place of corticosteroid therapy in chronic lymphatic leukaemia and related diseases accompanied by anaemia and a negative response to the Coombs test was studied in 20 patients admitted to the Massachusetts General Hospital, Boston, or Pondville Hospital, Walpole, Massachusetts. The diagnosis, based on the nomenclature of Gall and Mallory (*Amer. J. Path.*, 1942, **18**, 381), was chronic lymphocytic leukaemia in 14 and lymphocytic giant follicular or lymphoblastic malignant lymphoma in 6. None of the patients had obvious haemolytic anaemia and in all of them the results of erythrocyte survival studies and of bone-marrow examination suggested that in the genesis of the anaemia erythropoietic failure was more important than reduced erythrocyte life.

The standard treatment was 40 mg. of prednisone or 200 mg. of cortisone daily for 3 months, unless a definite response was obtained earlier. None of the patients responded to an initial dose lower than this standard dose. Several responded in 2 to 4 weeks and were then maintained on a smaller dosage, but most required 3 months of the standard regimen for a satisfactory

therapeutic effect. Of the 20 patients adequately treated by these standards, a good response (mean duration 18½ months) was obtained in 12 and limited improvement in 4; the remaining 4 responded unfavourably or not at all. Only in one successfully treated case was it possible to discontinue treatment without relapse, and that was after splenectomy. Generally, improvement was manifest by a rise in the haemoglobin level and in the reticulocyte and leucocyte counts with diminution in the size of the spleen and lymph nodes. A rise in the leucocyte count occurred in 17 cases, the exceptions being 3 cases of malignant lymphoma in which the leucocyte count was normal. The rise was due to mature lymphocytes, no immature cells being noted, and the count generally fell to something below the pre-treatment value after 2 to 4 months. Survival of labelled erythrocytes was estimated during treatment in 7 cases. The results, together with the observed effect of treatment on the reticulocyte count, are interpreted as indicating that the effect of corticosteroid therapy on the anaemia was due to stimulation of erythropoiesis rather than to increased erythrocyte life. The undesirable side-effects of the regimen are emphasized; because of these it is suggested that in the absence of obvious haemolysis corticosteroid therapy should be withheld until late in the course of the disease.

[The original paper should be read by all responsible for the management of patients with chronic lymphatic leukaemia and related diseases.] *A. G. Baikie*

765. **Leukaemia and Foetal Haemoglobin: a Case Study**
S. SHUSTER, J. H. JONES, and G. S. KILPATRICK. *British Medical Journal* [*Brit. med. J.*] **2**, 1556–1558, Nov. 26, 1960. 1 fig., 12 refs.

766. **Intracranial Bleeding in Hemophilia**
A. SILVERSTEIN. *Archives of Neurology* [*Arch. Neurol.*] **3**, 141–157, Aug., 1960. 1 fig., bibliography.

The author reviews the literature on the occurrence of haemorrhage within the cranial cavity in haemophilia, describes 11 new cases, and discusses the diagnosis and management of intracranial haemorrhage in haemophilic patients in the light of modern knowledge of both neurology and haematology. Haemophilia in its true or classic form is due to a deficiency of antihaemophilic globulin (A.H.G.), but deficiencies of plasma thromboplastin component (P.T.C., Christmas factor) or of plasma thromboplastin antecedent are classified as haemophiloid disease. The incidence of intracranial bleeding in haemophilia has been reported to be between 2·2% and 7·8%; in the haemophilic patients admitted to the Mount Sinai Hospital, New York, it occurred at some time in 6·3% (11 out of 174).

Of the 96 cases of probable intracranial bleeding reported in the literature and in this series, only 31 satisfied rigid criteria for proof of both the diagnosis of haemophilia and the occurrence of intracranial haemorrhage. Analysis of these 31 revealed that intracranial haemorrhage occurred mostly in haemophiliacs under 20 years of age, that previous head trauma was a significant aetiological factor, that convulsions occurred in more than half the patients, and that recurrent episodes were not uncommon. Intracranial bleeding was more likely to occur in patients with P.T.C. deficiency than in those with the classic haemophilia. The mortality was high, only 9 of the 31 patients surviving.

Illustrative cases are described to show that subarachnoid bleeding can be the first significant manifestation of a haemorrhagic diathesis, that provided plasma therapy has been given to try to maintain A.H.G. levels at 30% of normal lumbar puncture can be safely undertaken and should be performed on all haemophiliacs suspected of having intracranial bleeding, and that surgical intervention, with the possible exception of craniotomy for haemorrhage confined to the sub- or epidural spaces is unwise. Prophylactic anticonvulsant therapy should be administered to all haemophiliacs with intracranial bleeding. If a patient's condition deteriorates in spite of treatment cerebral arteriography may be justified and is preferable to trephination. Intracranial haemorrhage in haemophiliacs is usually sub- or epidural or intracerebral; subarachnoid bleeding when it occurs carries the best prognosis. *A. Ackroyd*

767. **Sporadic Hemophilia**
A. J. QUICK. *Archives of Internal Medicine* [*Arch. intern. Med.* (*Chicago*)] **106**, 335–340, Sept., 1960. 4 figs., 9 refs.

Evidence for the hypothesis that haemophilia may arise *de novo*—that is, by mutation, was examined at Marquette University School of Medicine, Milwaukee, several cases of sporadic haemophilia being studied. In one family in which 5 brothers were severe bleeders there was no history of haemophilia in three generations before the present one in spite of the large number of male members. In a second family there were bleeders in each of three generations and one carrier had 7 haemophilic sons. In a third family with male twins one of the twins was a moderately mild bleeder and the other was apparently normal; although the twins appeared to be identical it seemed probable that they were not monozygotic. In a fourth family, a typical haemophilic one, there were monozygotic twins, both of whom were bleeders.

The author states that the severity of haemophilia remains remarkably constant in any particular family and that this quantitative transmission of the defect is important in considering the probability of mutation. The finding in a girl of a bleeding state indistinguishable from that of a true haemophiliac (Quick and Hussey, *Lancet*, 1958, **1**, 1294; *Abstr. Wld Med.*, 1958, **24**, 356) presents a unique genetic enigma, the most probable explanation being that the girl was homozygous in regard to the haemophilic gene—that is, a mutation had arisen in both her X chromosomes. Further evidence for the occurrence of mutations is provided by the fact that neither the incidence of haemophilia A nor that of haemophilia B (Christmas disease) is decreasing. Moreover, the fairly constant ratio of haemophilia A to haemophilia B (5:1) suggests that the mutation rate for the former is higher than that for haemophilia B.
A. W. H. Foxell

Respiratory System

768. **Mediastinal Tumors and Cysts in the Adult**
M. JOANNIDES JR. and H. T. LANGSTON. *Diseases of the Chest* [*Dis. Chest*] **38**, 243–249, Sept., 1960. 4 figs., 16 refs.

The authors report their experience in 117 cases of proved mediastinal tumour or cyst seen at the Veterans Administration Hospital, Hines, Illinois, between 1932 and 1957; obvious cases of carcinoma of the lung or oesophagus and metastases from primary tumours elsewhere were excluded.

The patients in this series were, with one exception, men and were aged between 21 and 70 years. Of the lesions found, 27 were of mesenchymal origin (including 10 leiomyomata of the oesophagus and 2 diffuse malignant mesotheliomata), 22 were cysts (including 16 bronchogenic and 4 pericardial), 16 lymphomata (4 lymphosarcomata and 3 lymphoblastomata), 15 intrathoracic extensions from the thyroid (3 carcinomata and 8 benign adenomata), 11 teratomata (2 dermoid cysts and 2 malignant teratomata), 6 undiagnosed bronchial carcinomata, 5 neurogenic tumours, and 5 thymomata. There were also 4 aneurysms, a tumour of parathyroid origin, and 5 lesions classed as " miscellaneous ".

The authors stress that careful interpretation of good radiographs remains the most valuable tool in making a preoperative diagnosis of mediastinal neoplasm. However, owing to the diversity of histological types met with they feel that a specific diagnosis is unlikely, though they have found scalene-node biopsy particularly useful in diagnosing lymphomata, granulomata, and carcinomata. They therefore consider that early thoracotomy is advisable and that " delay for extensive diagnostic workup is usually not indicated ". *B. Golberg*

LUNGS AND BRONCHI

769. **Hyponatraemia and Impaired Renal Tubular Function with Carcinoma of Bronchus**
J. R. REES, S. B. ROSALKI, and A. D. W. MACLEAN. *Lancet* [*Lancet*] **2**, 1005–1009, Nov. 5, 1960. 1 fig., 12 refs.

770. **Effects of Pulmonary Hypertension of [*sic*] the Tracheobronchial Tree**
J. E. EDWARDS and H. B. BURCHELL. *Diseases of the Chest* [*Dis. Chest*] **38**, 272–284, Sept., 1960. 16 figs., 1 ref.

A study at the Mayo Clinic has shown that in cases of pulmonary hypertension without raised left atrial pressure the left pulmonary artery tends to push the aortic arch upwards and to the right, accentuating the aortic indentation on the left side of the trachea. The left main bronchus shows distortion downwards and to the right, resulting in a general, broad, downward concavity, with a possible localized indentation at the site of direct contact with the left pulmonary artery. At the bifurcation of the right main bronchus the dilated right lower pulmonary artery may push the right upper-lobe bronchus above and away from the intermediate bronchus below and may also compress both of them.

In cases with raised left atrial pressure there occur, in addition to the changes described above, others due to pressure and displacement by the atriomegaly. The angle of the tracheal bifurcation increases from the normal 90 degrees to almost 180 degrees, and the upward pressure against the lower aspect of the main bronchi tends to compress them and so facilitate their collapse. The right main bronchus rarely, if ever, shows changes, but the left may exhibit signs of considerable compression. In young children this may be responsible for obstructive emphysema or atelectasis and recurrent pulmonary infection. *B. Golberg*

771. **A Trial of Continuous Winter Chemotherapy in Chronic Bronchitis**
R. B. PRIDIE, N. DATTA, D. G. MASSEY, G. W. POOLE, J. SCHNEEWEISS, and P. STRADLING. *Lancet* [*Lancet*] **2**, 723–727, Oct. 1, 1960. 1 fig., 24 refs.

According to some observers long-continued prophylactic chemotherapy with tetracycline or penicillin reduces both the frequency and duration of exacerbations of chronic bronchitis. However, the results of the double-blind controlled trial here reported from the Hammersmith Chest Clinic, in which the effects on 151 chronic bronchitics of the daily administration during winter of (1) 0·5 g. of oxytetracycline (51), (2) 500 mg. of potassium phenoxymethylpenicillin together with 2 g. of the sulphonamide sulphadimidine in combined tablets (49), or (3) a placebo (51) were compared, do not confirm this.

At the end of 24 weeks no significant difference in regard to ventilatory function or to the proportion of patients showing reduction in degree of dyspnoea or change in exercise level was found in the three groups. The penicillin–sulphonamide group did show a steady and significant reduction in sputum volume during the first 4 months compared with the other two groups, and patients in this group more frequently claimed subjective improvement when recording their daily condition. Both treatment regimens brought about a small, not statistically significant, reduction in the duration of exacerbations and also reduced the incidence and number of *Streptococcus pneumoniae*, but not those of *Haemophilus influenzae*, isolated from the sputum, but the frequency of exacerbations was almost the same in all three groups. Only 10 of the 33 patients who withdrew from the trial had to do so because of toxic reactions, 7 of these being in the group receiving penicillin with sulphonamide.

A marked correlation was observed between a rise in concentration of smoke and sulphur dioxide in the

atmosphere and subjective deterioration of the patients, an adverse influence which is largely independent of chemotherapy. *A. Ackroyd*

772. **Fate of 424 Patients with Pneumonia and Bronchitis**

J. FRY. *British Medical Journal* [*Brit. med. J.*] **2**, 1483–1486, Nov. 19, 1960. 3 refs.

424 patients who suffered from pneumonia or acute bronchitis in 1949–54 were followed up for 5 to 10 years and reassessed functionally in 1959. As many as 43% were considered to be disabled according to the method of grading used, 9% were complete invalids, and 24 had died during the acute illness. This rate of disability was more than twice that present (21%) before the infection 5 to 10 years earlier.

Three distinct clinical conditions were recognized—lobar pneumonia, segmental pneumonia, and acute bronchitis. Lobar pneumonia accounted for 15% of the whole series. The age incidence rose with age. The sex distribution was equal. It was more frequent in lower social groups, in male smokers, and in those with a previous history of chest illness. There was a disability rate of 42%, compared with 21% before the episode. Segmental pneumonias were much the most frequent in young children. There was a disability rate at follow-up of only 16%, and some relations were noted with social classes and smoking; even this rate was much higher than the 6% before the infection. Acute bronchitis had the unusual age incidence of being frequent in the young and the old. Disability at follow-up had occurred in 71%, and there were close associations with smoking, social classes, and previous chest illnesses. The initial disability rate had been 38%.

The importance of acute chest illnesses is evident from the fact that one million persons are affected each year and that 43% appear to be left with some disability, which is twice the initial figure. Preventive measures must take into account the associations between disability and age, sex, social class, smoking habits, past history, and environmental and genetic influences.—[Author's summary.]

773. **A Maintenance Trial of Combined Steroid and Antibiotic Treatment in a Series of Asthmatics with Chronic Bronchitis**

A. G. OGILVIE and D. J. NEWELL. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **54**, 308–320, Oct., 1960. 25 refs.

In a previous survey carried out in Newcastle upon Tyne the authors found that asthma was significantly more prevalent among patients with chronic bronchitis than among those not so affected, 42 (9%) of 464 bronchitics being asthmatic as against 5 (1%) of 485 non-bronchitics. Several authors have reported that worthwhile improvement can be obtained in chronic bronchitics by the daily administration of tetracycline over prolonged periods. In view of the frequent association of asthma with chronic bronchitis and the considerable loss to the patients and to industry occasioned thereby the present authors considered that a trial of combined treatment with a steroid and an antibiotic was needed in an attempt to relate the cost of such maintenance treatment to the gain achieved by enabling the patients to remain at work.

For this investigation only men under the age of 60 suffering from persistent asthma and chronic bronchitis were selected. They were treated by a combined regimen of "albamycin T", an antibiotic containing equal proportions of novobiocin and "terramycin" (oxytetracycline), in a dosage of 0·5 g. twice a day and either a tablet of methylprednisolone ("medrone"), 4 mg. three times a day, or a similar dummy tablet over a period of 4 winter months, the allocation to medrone or the dummy tablet being by random selection. The criteria for the diagnosis of chronic bronchitis and for inclusion in the trial are described. Clinical analysis of the cases showed a strong personal and/or hereditary allergic background. The sole criterion of improvement recognized was a reduction in the amount of sick absence during the trial period as compared with that in the corresponding months of the two preceding winters. In addition, all patients were given a diary in which they marked standard phrases recording their state of health and their presence at or absence from work.

During the 4-month trial, which was completed by 60 men, 18 showed severe clinical detericration. In 15 of these cases it was necessary to change from dummy tablets to prednisolone; 9 of the 15 had been taking this steroid before the trial but had been allocated by chance to the dummy tablets, and there was strong suggestive evidence that the respiratory deterioration in these subjects was related to cessation of steroid treatment on entry to the trial. Discrepancies between the records kept by the patients and those supplied by the Ministry of Pensions and National Insurance regarding absence from work were numerous and applied to some 20% of the cases. The result of the trial was affected by this discrepancy, but even had the most favourable estimate been accepted the economic gain would have been relatively slight in view of the present cost of medrone.

The authors further conclude that in future similar trials it would be inadvisable to rely on diaries kept by patients in assessing the amount of work lost through illness. *A. J. Karlish*

774. **Lung Biopsy in Sarcoidosis: with Special Reference to Bacteriological and Microscopic Features**

L. REID and G. LORRIMAN. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **54**, 321–334, Oct., 1960. 12 figs., 28 refs.

In this paper from the Brompton Hospital, London, the clinical, radiographic, and pathological findings are reported in 16 cases of sarcoidosis, the diagnosis of which was confirmed by means of lung biopsy carried out through a limited thoracotomy incision as described by Klassen *et al.* (*Arch. Surg.* (*Chicago*), 1949, **59**, 694; *Abstr. Wld Surg.*, 1950, **7**, 122). In one patient, a 21-year-old-girl who developed a right-sided pleural effusion in 1951, there was strong evidence of a tuberculous aetiology. The only additional radiographic abnormality

at that time had been a calcified scar at the left apex. Pleural fluid was negative on culture for *Mycobacterium tuberculosis* and the Mantoux reaction was negative to 1 t.u. (the only strength used). The effusion was quickly absorbed, but in 1952 patchy infiltration developed throughout both lung fields. In 1953 the Mantoux reaction was negative to 100 t.u., but a gastric lavage gave a positive culture of *Myco. tuberculosis*. At thoracotomy her lung was found to be studded with numerous firm nodules, 2 to 15 mm. in diameter, and a biopsy specimen taken from the middle lobe showed several sarcoidal lesions, the largest being 2 mm. in diameter. Culture of a portion of the specimen was positive for *Myco. tuberculosis*. Injection of a further portion into a guinea-pig did not produce generalized tuberculosis, but tubercle bacilli were cultured from pus aspirated from an inguinal gland of this animal. Treatment of the patient with a 6-week course of streptomycin had no noticeable effect on the radiographic abnormalities.

In another patient, a woman aged 23 who gave a negative Mantoux reaction to 100 t.u., lung biopsy showed numerous granulomata characteristic of sarcoid. Sputum was repeatedly negative on culture for acid-fast bacilli, but 4 years later there was a slight increase in the radiographic extent of infiltration and one of 6 samples of sputum gave a positive culture for *Myco. tuberculosis*, the Mantoux reaction remaining negative to 100 t.u. The authors note that the finding of *Myco. tuberculosis* in patients with sarcoidosis is by no means rare; Scadding reported recovering *Myco. tuberculosis* from 14 out of 142 such patients.

In 2 other patients necrosis resembling caseation was found in excised hilar lymph nodes; true caseation was, however, excluded by the use of van Gieson's stain for collagen and Gomori's stain for reticulum. In a fifth patient the pathological changes preceded radiographic abnormalities by several months. It is concluded that the findings in this series suggest that biopsy of the lung with simultaneous excision of a hilar node will give a positive diagnosis in practically all patients with sarcoidosis and lung involvement. In particular, lung biopsy is more likely to be successful than liver biopsy in those patients whose chest radiographs show diffuse pulmonary infiltration without evidence of hilar lymph-node enlargement. *A. J. Karlish*

775. **Combined Antibiotic–Haemotherapy Treatment of Bronchiectasis and Lung Abscess.** (Лечение бронхоэктатической болезни и абсцесса легких антибиотиками в сочетании с гемотерапией)
P. M. Al'perin, M. Ja. Anševic, I. B. Gurevič, V. E. Krupjanko, O. P. Melehova, and R. I. Rodina. *Советская Медицина* [*Sovetsk. Med.*] **24**, 51–56, Sept., 1960. 12 refs.

The authors describe the results in 52 patients admitted to hospital with exacerbation of bronchiectasis and in 22 with chronic lung abscess who were given antibiotics systemically, mostly penicillin but in some streptomycin, chlortetracycline, or chloramphenicol. Penicillin, with or without streptomycin, was also administered locally by bronchoscopy or intratracheal catheterization or as an aerosol twice a week. In addition, when drainage had been established the patients were given 2 to 4 transfusions of packed cells (rarely whole blood) in doses varying from 100 to 250 ml. at intervals of 4 to 6 days, this being often supplemented by plasma and in a few cases by transfusions of an alcohol–glucose–albumin solution.

Of the 22 patients with lung abscess, 15 were cured and 3 improved; treatment failed in 4 patients, in 2 because they discharged themselves before the treatment was completed, while in the other 2 drainage could not be established because of the peripheral position of the cavity. It was noted that in chronic cases haemotherapy undoubtedly helped by increasing the general bodily reactivity. Of the 52 patients with bronchiectasis, 50 improved, 27 of them considerably. One patient with diffuse bilateral disease and amyloidosis died. The authors consider that the combination of antibiotics with haemotherapy resulted in a quicker return of the blood picture to normal than with antibiotics alone, more prompt relief of oxygen starvation, and faster restoration of the respiratory, renal, and hepatic functions and the haemodynamic indices, while the improvement in the radiological and electrocardiographic findings was more stable. *S. W. Waydenfeld*

776. **Potential Harmful Effects of Treating Pulmonary Encephalopathy with a Carbon Dioxide Buffering Agent**
A. G. Swanson. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **240**, 433–437, Oct., 1960. 1 fig., 4 refs.

Tris(hydroxymethyl)aminomethane is an organic buffering agent which combines with carbonic acid to form a bicarbonate complex, thereby lowering the carbon dioxide tension and raising the *p*H of the blood. These properties suggested that "tris" might be of value in the treatment of encephalopathy accompanying carbon dioxide retention in man. However, before giving the drug to patients severely ill with pulmonary encephalopathy the author of this paper from the University of Washington School of Medicine, Seattle, studied the effect of rapid intravenous infusion of tris in 3 patients with compensated CO_2 retention.

A reduction in the CO_2 tension in arterial blood, a rise in the blood *p*H, and profound hypoventilation occurred in all 3 patients. Minute ventilation fell by 40% in the 2 patients in which this was determined. A significant fall in the arterial oxygen saturation and, because of alkalosis, an even more profound fall in the arterial oxygen partial pressure were seen in all cases. This hypoventilation was thought to be due to the combination of tris with free CO_2 with reduction of the stimulation of breathing. Although these 3 patients suffered no harmful effects (other than tremulousness and agitation in one) it is considered that the anoxaemia produced is potentially harmful and precludes the use of tris in this way, at least in patients with pulmonary encephalopathy. *A. Gordon Beckett*

Otorhinolaryngology

777. **Otosclerosis with Bilateral Stapes Mobilization: Histological and Clinical Considerations**
F. ALTMANN, M. BASEK, and J. V. HOUGH. *Archives of Otolaryngology* [*Arch. Otolaryng.*] **72**, 147–162, Aug., 1960. 14 figs., 26 refs.

From the results of their histological examination of the middle ear and temporal bones of patients who died at various periods after mobilization of the stapes for otosclerosis the authors consider that re-growth of bone through the lesion occurs in some 50% of cases, especially if the annular ligament is damaged. In their view Fowler's " crurotomy " gives better results, but this operation is possible in only a comparatively small number of cases. At present the most promising method seems to be removal of the stapes, with closure of the window by a vein graft and reconstruction of the ossicular chain. It has yet to be seen whether the otosclerotic focus can invade the graft, and how well the labyrinth will tolerate the presence of a foreign body. Fortunately the labyrinth appears to have a considerable power of resistance. The mobilization operation is described as " rather haphazardous and unpredictable ".

F. W. Watkyn-Thomas

778. **Viral Pneumonia of the Mother with Hemorrhagic Otitis in the Fetus**
G. KELEMAN and J. H. NEAME. *Archives of Otolaryngology* [*Arch. Otolaryng.*] **72**, 163–169, Aug., 1960. 6 figs., 13 refs.

The possibility that maternal influenzal infection may be a cause of congenital deafness in the infant is discussed in this paper from Harvard Medical School and Massachusetts Eye and Ear Infirmary, with reference to the case of a woman aged 20 who died in the 23rd week of her first pregnancy after she had contracted pneumonia, in the course of which influenza-A virus (Asiatic strain) was isolated from her throat. Necropsy was performed on the foetus within 3 hours, but no virus was detected. However, among many other pathological signs, the temporal bones showed a haemorrhagic otitis of influenzal type.

The authors discuss the various factors involved and give a warning that caution is needed in interpreting the findings.

F. W. Watkyn-Thomas

779. **Etiology of Unilateral Total Deafness Studied in a Series of Children and Young Adults**
G. EVERBERG. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **69**, 711–730, Sept., 1960. 2 figs., 36 refs.

Unilateral total deafness was studied in 122 children and young adults at the Copenhagen City Hospital. A hereditary factor was found in 25%, and in 9% radiological investigation showed developmental anomalies. In a further 17% the deafness seemed to have been acquired, the commonest cause being meningitis, followed by mumps, labyrinthitis, and head injury. No cause for the deafness was found in 50% of the patients.

William McKenzie

780. **The Role of Radiation Therapy in Carcinoma of the Larynx**
J. L. GOLDMAN and S. M. SILVERSTONE. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **69**, 890–905, Sept., 1960. 1 fig., 25 refs.

During the years 1931–54 312 cases of laryngeal and laryngopharyngeal carcinoma were treated by irradiation at Mount Sinai Hospital, New York. Of 43 patients in whom the carcinoma was limited to the vocal cord, 9 were lost to follow-up or died from other causes (" indeterminate " cases); 30 (88%) of the remaining 34 survived 5 years. Of 94 cases of more extensive intrinsic carcinoma, 21 were classed as " indeterminate ", the survival rate in the remaining 73 being 63% (46 cases). Of 115 cases of extrinsic carcinoma, the growth was anterior in 53 and posterolateral in 36, while in 26 both locations were involved. The 5-year survival rates in these 3 groups (excluding " indeterminate " cases) were 25 out of 45 (56%), 9 out of 28 (32%), and 3 out of 21 (14%) respectively. If the " indeterminate " cases were all regarded as failures the rates for the 5 groups became 70%, 49%, 47%, 25%, and 11% respectively. The prognosis depends partly on whether the lymph nodes are affected, this being most frequent in extrinsic carcinoma involving the posterolateral area. In such cases the authors recommend combined surgery and radiotherapy, operation, including removal of the lymph nodes, being performed 3 to 6 weeks after completion of ^{60}Co teletherapy.

William McKenzie

781. **Inner Ear Pathology in Deafness Due to Mumps**
J. R. LINDSAY, P. R. DAVEY, and P. H. WARD. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **69**, 918–935, Sept., 1960. 6 figs., 32 refs.

So far as the authors could discover this is the first recorded case of deafness due to mumps in which the pathological changes in the temporal bones have been studied after death. The patient developed mumps at the age of 2 and died 4 years later from nephritis. The temporal bones were removed and taken to the University of Chicago for examination. In the cochlea was found atrophy of the stria vascularis, tectorial membrane, and organ of Corti. The change was confined to the endolymphatic system, and the authors consider it to be due to a labyrinthitis caused by the mumps virus.

William McKenzie

782. **Tumors of the Nose and Throat**
K. D. DEVINE. *Archives of Otolaryngology* [*Arch. Otolaryng.*] **73**, 80–124, Jan., 1961. Bibliography.

Urogenital System

783. **The Use of Norethandrolone in Acute Renal Failure from Obstetric Causes**
C. R. Blagg and F. M. Parsons. *Lancet* [*Lancet*] **2**, 577–581, Sept. 10, 1960. 6 figs., 21 refs.

This report from the artificial-kidney unit at the General Infirmary at Leeds concerns 19 women who developed acute renal failure following complications of pregnancy. As infection is known to increase the rate of protein catabolism no infected patient was included in the study. Of the 19 patients, 3 served as controls and 16 were treated with anabolic steroid drugs in addition to the usual medical measures, which included haemodialysis as required. All patients received 100 g. of glucose per day in 400 ml. of water, and sensible water loss was replaced as it occurred.

The plasma and urinary urea levels were determined daily and total urea production estimated by adding the amount excreted in the urine (if any) to that accumulating in the total body water. Norethandrolone reduced the average rate of urea production by 70%, which exceeded the reduction following the administration of testosterone or progesterone and was as great as that following testosterone and progesterone given together. Oral doses of 30 mg. or 80 mg. of norethandrolone and intramuscular doses of 50 mg. or 100 mg. per day produced approximately equal effects. No virilization, jaundice, or other side-effects were noted in any of the patients receiving norethandrolone.

It is suggested that the apparent anabolic action of these drugs is in fact anti-catabolic. *T. B. Begg*

784. **Treatment of Urinary Infections with Cycloserine**
R. W. Fairbrother and G. Garrett. *British Medical Journal* [*Brit. med. J.*] **2**, 1191–1194, Oct. 22, 1960.

Cycloserine was tried at Manchester Royal Infirmary in the treatment of 22 patients with infections of the urinary tract, the drug being given in a dosage of 250 mg. 6-hourly for an average period of 7 days. Cycloserine is largely concentrated in the urine, and a steady urinary level was achieved, the mean concentration being about 600 μg. per ml.

The sensitivity of 334 organisms freshly isolated from urinary infections was determined *in vitro*. Of these, 110, mainly *Proteus* or *Pseudomonas pyocyanea*, were inhibited only by cycloserine concentrations of 640 μg. per ml. or more, while only 113 were inhibited by 160 μg. per ml. or less. Resistance readily developed *in vitro*, but was not a problem during the treatment of patients.

Of the 22 patients, only 3 were cured, all these having infections due to strains of *Escherichia coli* sensitive to several antibiotics; in 6 further patients there was temporary improvement, with relapse within 48 hours of cessation of treatment. The drug had to be withdrawn in 4 cases because of vertigo and drowsiness.
David Phear

785. **The Renal and Urinary Changes in So-called Haemorrhagic Nephroso-nephritis** (О почечно-мочевом синдроме при так называемом геморрагическом нефрозо-нефрите)
A. G. Kestner. *Архив Патологии* [*Arh. Patol.*] **22**, 12–20, No. 9, 1960. 6 figs., 1 ref.

Discussing the post-mortem changes found in patients dying of so-called haemorrhagic nephroso-nephritis the author states that from the first days of illness there is usually a reduction in the volume of urine (to 500 ml. to 800 ml. daily) with a rise in its specific gravity. This first stage of the disease is accompanied by fever, headache, abdominal pains, hiccup, and vomiting and lasts usually about 6 days. Thereafter the temperature falls, the symptoms become more severe, and marked oliguria and albuminuria supervene. The mortality varies from 2% to 20% or even higher. At necropsy the kidneys are found to be swollen and haemorrhagic, and on cross-section apoplexy of the medullary substance is observed, while in 8 of the 22 cases examined by the author there were capsular tears. Histologically, the essential renal lesion is an extreme degree of congestion, especially in the medulla, with consequent compression of the renal tubules, venous thrombosis, and occasional cortical infarcts. The primary lesion is believed to be in the hypothalamic region of the brain and the hypophysis.
A. Swan

786. **On Renal Papillary Necrosis with Special Reference to the Diagnostic Importance of Papillary Fragments in the Urine, Therapy (i.a. Artificial Kidney) and Prognosis. Report of 75 Cases, Including 12 with Papillary Fragments in the Urine.** [In English]
T. Lindholm. *Acta medica Scandinavica* [*Acta med. scand.*] **167**, 319–330, 1960. 3 figs., 21 refs.

Between 1947 and 1959 75 cases of renal papillary necrosis were diagnosed at the University Medical Clinic, Lund, Sweden. In 63 cases the diagnosis was established by radiological examination or at necropsy, while in the remaining 12 it could be made when necrotic papillary fragments were found in the urine. In 6 of these cases pyelography revealed findings typical of papillary necrosis. The papillary fragments were usually detected when the urine was filtered in the investigation of a " renal colic ". It is recommended that this procedure should always be performed in patients with chronic pyelonephritis in whom attacks of pain cannot be explained by finding " radio-opaque concrement ". The case histories of these 12 patients are presented. They received intensive antibiotic therapy for the urinary tract infection, sometimes for many months. The prognosis appears to be better than has been thought hitherto. Only 2 of the 12 patients died, while in 4 cases the treatment led to healing of the pyelonephrosis. The incidence of diabetes mellitus in this series was not particularly high—10 cases or 13·3%. *G. W. Csonka*

Endocrinology

787. **Psycho-endocrinology of Klinefelter's Syndrome.** (Beitrag zur Psychoendokrinologie des Klinefelter-Syndroms)
K. DENGLER. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **200**, 626–638, 1960. 3 figs., 14 refs.

The author describes the case of a 21-year-old male patient whose chromosomal sex was female and who showed mild feminine secondary sex characteristics such as gynaecomastia, feminine distribution of pubic hair, and body measurements. The urine showed reduced excretion of androgens and increased excretion of oestrogens. The patient was treated with choriongonadotrophin, a total of 172,000 units being given over 3 months, together with subcutaneous injections of testosterone to a total of 4,500 mg. As a result he became more settled and showed heterosexual interests for the first time in his life. It was interesting that during treatment this man exhibited a type of sulky behaviour characteristic of adolescents which disappeared as the treatment progressed. *J. Hoenig*

788. **Study of the Adrenal Response to ACTH after Prolonged Treatment with Prednisone Alone or in Combination with ACTH or Testosterone.** (Étude de la réponse surrénalienne à l'A.C.T.H. après traitement prolongé par la delta-cortisone associée ou non à l'A.C.T.H.-retard ou à la testostérone)
J. BERTRAND, J. MAITREPIERRE, and B. LORAS. *Revue française d'études cliniques et biologiques* [*Rev. franç. Ét. clin. biol.*] **5**, 684–690, Aug.–Sept., 1960. 7 figs., 40 refs.

It is known that after prolonged treatment with corticosteroids the adrenal cortex responds subnormally to stimulation with ACTH (corticotrophin). The experiments reported in this paper from the Institut Pasteur, Lyons, were designed to determine the duration of this insufficiency and whether it could be prevented or reduced by including ACTH or testosterone in the therapeutic regimen. The plasma 17-hydroxycorticosteroid levels were first determined at 0, 2, 4, and 6 hours during the intravenous infusion of 25 mg. of ACTH in 33 healthy subjects, thus establishing the normal response to such an infusion of ACTH.

A similar infusion of ACTH given to 34 patients 12 hours after cessation of treatment with prednisone alone for various periods, ranging from 20 days to 10 months, gave a uniformly subnormal response. When the test infusion was delayed for 36 hours after cessation of treatment with prednisone 4 out of 6 patients gave a subnormal response, and when 60 hours were allowed to elapse before the test infusion, 3 out of 6 patients gave a subnormal response. Of a third group of 6 patients only 2 gave a subnormal response when 6½ days were allowed to elapse between cessation of treatment and the test infusion, while of 6 patients who received 15 to 20 mg. of prednisone daily for periods ranging from 19 days to 3½ months supplemented by 50 mg. of testosterone every 5th or 7th day, all gave a subnormal response to the test infusion of ACTH given at 12 hours. However, when treatment with prednisone was supplemented with 20 mg. of ACTH-zinc (a retard preparation) every 5th or 7th day the response to the test 12 hours after cessation of the treatment was normal in 4 out of 6 patients. *P. A. Nasmyth*

[An English translation of this paper was published simultaneously in the U.S.A. (*J. Pediat.*, 1960, **57**, 471). No acknowledgment of this fact is made in either journal. —EDITOR.]

THYROID GLAND

789. **Stable Iodine Metabolism in Non-toxic Goitre**
D. A. KOUTRAS, W. D. ALEXANDER, W. W. BUCHANAN, J. CROOKS, and E. J. WAYNE. *Lancet* [*Lancet*] **2**, 784–787, Oct. 8, 1960. 1 fig., 22 refs.

At the Western Infirmary, Glasgow, the authors studied the total iodine metabolism in 21 patients with sporadic goitre and in 13 healthy individuals; the procedure included determination of the plasma inorganic iodine level, so that from this value and the other usual factors the absolute uptake of iodine by the thyroid gland could be calculated.

Low plasma inorganic iodine levels (0·02 to 0·09 μg. per 100 ml.) were found in 16 of the patients with non-toxic goitre, while the other 5 had low-normal levels. The 24-hour urinary excretion of iodine was significantly lower in the goitrous patients, and they showed no evidence of decreased absorption or increased excretion of iodine. Thyroid clearance of iodine varied inversely with plasma inorganic iodine levels, thus acting as a compensatory mechanism serving to keep the absolute uptake of iodine by the thyroid within normal limits. From the results of this study the authors conclude that a low iodine intake is one of the causative factors in the aetiology of sporadic non-toxic goitre, the incidence of which could thus be reduced by the iodination of household salt. *F. W. Chattaway*

790. **Stable Iodine Metabolism in Thyroid Dyshormonogenesis**
D. A. KOUTRAS, W. D. ALEXANDER, W. W. BUCHANAN, J. CROOKS, and E. J. WAYNE. *Scottish Medical Journal* [*Scot. med. J.*] **5**, 331–334, Aug., 1960. 1 fig., 8 refs.

At the Western Infirmary, Glasgow, stable iodine metabolism was studied in 4 patients, siblings, suffering from thyroid dyshormonogenesis. Of the 4 patients (1 male and 3 female, aged 45 to 54 years) 3, who were goitrous deaf-mutes, had impaired ability to utilize trapped iodide (peroxidase deficiency), while the fourth

was a goitrous cretin with a high proportion of butanol-inextractable protein-bound iodine in the plasma. In all 4 cases the absolute iodine uptake (A.I.U.) was raised, figures of 21·5 to 28·2 μg. per hour being recorded, compared with a normal range of 1 to 6 μg. per hour. The thyroid clearance was also high—55·4 to 346 ml. per minute compared with normal values of 6 to 40 ml. per minute. The serum protein-bound iodine (P.B.I.) level was normal or low, values of 3·1 to 7 μg. per 100 ml. being recorded, while the plasma inorganic iodine level was normal.

The authors point out that in all 4 cases the combination of a high A.I.U. with a normal P.B.I. level demonstrates that there was faulty utilization of iodine by the thyroid, consistent with enzyme defects known to occur in dyshormonogenesis. This can be shown numerically by measuring what they term the "iodine utilization index", expressed as the ratio of the P.B.I. level to A.I.U. Normally, this figure lies between 1·0 and 6·6. In all 4 cases the index was low—0·13, 0·13, 0·4, and 0·3 respectively. It is suggested that the pattern of high radioactive iodine clearance, normal plasma inorganic iodine level, a high A.I.U., and a normal or low P.B.I. level is characteristic of goitre due to dyshormonogenesis, and so distinguishes it from iodine-deficient goitre, in which the radioactive iodine clearance is high, the plasma inorganic iodine level is low, and the A.I.U. and P.B.I. value are normal. *D. G. Adamson*

791. **Examination of Thyroid Activity with Radioiodine. The Mackenzie Davidson Memorial Lecture**
E. E. Pochin. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 595–605, Oct., 1960. 4 figs., bibliography.

792. **Reserpine and 6-Methylthiouracil in the Treatment of Thyrotoxicosis.** (Лечение больных тиреотоксикозом резерпином в комбинации с 6-метилтиоурацилом)
S. P. Čuba. *Терапевтический Архив* [*Ter. Arh.*] **32**, 76–80, Sept., 1960. 13 refs.

Reserpine has no direct effect on the thyroid gland, but by virtue of its sedative, sympatholytic, parasympathomimetic, and ganglion-blocking actions it favourably influences the disturbance of nervous function which is always present in thyrotoxicosis. Of 184 ambulatory patients who were treated with this drug, together with 6-methythiouracil, the disease was severe in 38·6%, moderately severe in 42·4%, and mild in 19%. The goitre, which was diffuse in 153 and mixed in 31 cases, was of Grade I in 9, Grade II in 39, Grade III in 114, and Grade IV in 22 patients. The investigations included electrocardiography, oscillography, and "clino-orthostatic" tests. The initial dosage of reserpine was 0·25 mg. twice a day, and if well tolerated this was increased after 3 or 4 days to 0·25 mg. three times a day and continued at this level until the therapeutic effect became apparent, when it was gradually reduced to a maintenance dose of 0·125 to 0·25 mg. daily. During administration of reserpine the dose of methylthiouracil required by the patients could be lowered and therefore the side-effects of this drug were less than when it was given alone in higher doses.

The treatment induced a remission in 76·8% of the patients, with a reduction in the size of the goitre and a recovery of working capacity; a further 14·3% improved considerably, although the reduction in goitre size was slow and some tendency to exacerbations of the disease persisted. Some improvement occurred in 6·5%, but the goitre failed to diminish and in some cases actually increased and exacerbations were frequent, while the remaining 2·4% of patients failed to respond to treatment. During the uninterrupted course of treatment (one year or more) the total doses were 35 to 85 mg. of reserpine and 20 to 65 g. or more of methylthiouracil. Reserpine was also successfully used in the preoperative treatment of patients refractory to iodine and in patients with severe cardio-circulatory disturbance. Side-effects attributable to reserpine were rare and transient and disappeared on adjustment of the dose.
S. W. Waydenfeld

793. **The Diagnosis of Malignant Tumours of the Thyroid Gland.** (К вопросу о диагностике злокачественных новообразований щитовидной железы)
Ja. V. Ermulovič and Ju. G. Kudinskij. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **6**, 81–88, Sept.–Oct., 1960. 3 figs., 36 refs.

Although formerly regarded as a rare disease, malignant tumour of the thyroid gland has in the past decade increased in frequency, the relative proportion rising from about 1% to between 5 and 10% of all diseases of the gland, while if the number of cases of malignant change is compared with the number of nodular goitres the ratio is still higher. In this paper the diagnosis of malignant disease of the thyroid is discussed with reference to 29 cases, 26 in women and 3 in men, of whom 22 were over 50 years of age. In 24 cases there was a previous history of thyroid abnormality.

The presenting symptoms were the presence of a tumour (17 cases), loss of weight (2), general weakness (6), cyanosis of the face (2), radiating pains towards the nape of the neck or ear (6), dyspnoea (10), dysphagia (9), hoarseness of the voice (8), and enlarged cervical lymph nodes (7). The last-named was a late sign and was seen only in advanced or neglected cases; the absence of this sign is therefore no reason for rejecting a diagnosis of malignant change. Like dyspnoea, dysphagia, and hoarseness it plays no part in the diagnosis of early cases, which should be based on the rapid increase in size, hardness, and lack of clear demarcation of the swelling. Capillaroscopy and biopsy examination should be carried out at the first suspicion of malignancy. The latter can be performed by smear or puncture at the time of operation, and from microscopical examination of a slide stained by the Giemsa–Romanovsky method the diagnosis can be made in a few minutes. One of the characteristic findings in sections or smears of malignant thyroid tissue is the presence of large multinuclear cells with striped protoplasm; another is the presence of small clumps of lymphoid cells of round or oval form with large nuclei and a scarcely visible rim of cytoplasm.

Yet another characteristic finding is an epithelial cell, 8 to 10 μ in diameter, with pale, blue-grey cytoplasm, a bean-shaped nucleus, and tail-like outgrowths.

The authors conclude that the early clinical diagnosis of malignant change in the thyroid is difficult. They recommend that in view of the tendency of nodular goitre to become malignant such goitres should be removed and conservative treatment not prolonged; furthermore, that such cases should be under observation at intervals for some years after operation.

L. Firman-Edwards

DIABETES MELLITUS

794. **A New Method for the Diagnosis of Diabetes. The Staub–Traugott Test with Corticotrophin.** (Contribution au diagnostic du diabète (une nouvelle méthode: épreuve de Staub–Traugott + A.C.T.H.))

B. DA COSTA. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **49**, 925–941, July–Aug., 1960. 12 figs.

Writing from the Faculty of Medicine of Coïmbra, Portugal, the author describes a new method for the diagnosis of diabetes based on a modification of the Staub–Traugott glucose tolerance test. The latter consists in plotting the blood sugar curves after giving two doses of glucose separated by an interval. In the normal individual the second curve is lower than the first because the pancreas responds to the first dose of glucose by secreting too much insulin, which results in lowering of the second curve. In the diabetic, however, most of the available insulin is used up in dealing with the first dose of glucose, so little is left to counteract the hyperglycaemia resulting from the second dose. The author's modification of the test consists in giving the patient 100 units of ACTH (corticotrophin) 2 hours before performing the Staub–Traugott test. The resulting curves are similar in pattern to those in the test without ACTH except that they are higher because of the increased sensitivity of the test; as before, the result is considered diagnostic of diabetes when the second curve is higher than the first. The new method is a very sensitive one and may give a positive result in a certain number of non-diabetic conditions. Nevertheless it is claimed to be a useful method in doubtful cases, prediabetic conditions, and cases of latent diabetes.

A. I. Suchett-Kaye

795. **Preliminary Observations on Management of Diabetes with "Stabinol"**

M. F. HEALY and J. D. ARNEAUD. *British Medical Journal* [*Brit. med. J.*] **2**, 913–915, Sept. 24, 1960. 7 refs.

The oral treatment of diabetes has special value in countries such as the British West Indies where many patients are afraid or are unwilling to learn to give themselves injections of insulin and so have to attend daily at the clinic, which for various reasons they are often unable to do regularly. The authors report, from the General Hospital, Port of Spain, Trinidad, a trial of the methoxy-*iso*butyl substituted thiadiazole known as FWH 114 or "stabinol" in 33 diabetics attending as out-patients. All but 2 had been having treatment with insulin and were selected on the basis of the insulin dosage being between 12 and 52 units per day. The age range was from 34 to 72, but the majority (20) were between 41 and 60 years of age. In all cases, irrespective of the previous dosage of insulin, the initial dosage of stabinol was four 250-mg. tablets daily given in a single dose in the morning.

Of the 30 patients who completed the trial, 15 were better controlled with stabinol than they had previously been with insulin, 9 were controlled equally well, and 6 were less well controlled; all but one of the patients expressed a preference for the tablet form of treatment. Liver function studies (using 5 of the usual tests) and the findings in the blood and urine remained normal throughout the study, and there were no side-effects or abnormal reactions. In view of these last observations the authors consider stabinol to be a safe and worth-while addition to the oral treatment of diabetes.

K. O. Black

796. **Experience of Chlorpropamide in 100 Cases of Diabetes Mellitus**

M. W. J. BOYD and A. P. GRANT. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] 408–421, Sept., 1960. Bibliography.

An analysis is presented from the City Hospital, Belfast, of the results of the treatment with chlorpropamide of 62 female and 38 male diabetics judged suitable for this type of therapy; their age range was 22 to 83 years, but only 3 were under 44. All were admitted to hospital for initial treatment, either because they were new patients or because the diabetes had been unsatisfactorily controlled by diet, with or without the addition of insulin. The initial dose of chlorpropamide was 500 mg. daily, followed in most cases by a maintenance dose of 250 mg. daily. Only rarely were larger doses used and these were seldom more effective.

A good or excellent response was obtained in 71 cases, that is, in 43 (70%) of the women and 28 (74%) of the men. Both the patients who were under the age of 40 at the time of onset failed to respond, developing ketosis, but some failures occurred in all age groups with onset up to the age of 68. However, advance in age was not found to reduce responsiveness. Overweight or obese patients did not respond so well, only 21 out of 47 (45%) of them achieving an excellent response, compared with 31 (69%) of 45 of normal weight. Side-effects, which were uncommon, included itchy dermatitis, becoming almost exfoliative, mild leucopenia, and heartburn. Three developed proven hypoglycaemia, and this was suspected in a further 10. Of the 18 patients showing a poor or only fair response, this was attributable to poor cooperation in 10 and in the others to poor subsequent attendance, poor intelligence, or poor living conditions. The literature is extensively reviewed.

A. Gordon Beckett

797. **Idiopathic Hyperlipemia and Diabetes Mellitus. Deviations from Normal Lipid Metabolism.** [A Review]

D. R. JACOBS. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **27**, 488–511, Sept.–Oct., 1960. Bibliography.

The Rheumatic Diseases

798. **Cerebrovascular Accidents in Rheumatic Fever.** (Сосудистые церебральные катастрофы при ревматизме)
V. V. Miheev. *Советская Медицина* [*Sovetsk. Med.*] **24**, 31–36, Sept., 1960.

Rheumatic fever may occasionally be complicated by various types of cerebrovascular accident, such as thrombosis, non-thrombotic softening, subarachnoid haemorrhage, cerebral haemorrhage, and less often cerebral embolism. Since any of the cerebral arteries may be affected the clinical picture is highly variable. In the absence of evidence of hypertensive disease or of syphilis an erroneous diagnosis may easily be made. The author states that cerebrovascular complications occur more often and are more severe in rheumatic fever than in other collagen diseases, probably owing to its protracted course and associated cardiac lesions. The condition must be differentiated from infections of the central nervous system, aneurysm, or influenzal haemorrhagic encephalitis. *S. W. Waydenfeld*

799. **The Latex Slide Test in Rheumatic Disorders**
J. V. Wilson, R. A. H. Morison, and V. Wright. *Journal of Clinical Pathology* [*J. clin. Path.*] **13**, 453–455, Sept., 1960. 1 fig., 16 refs.

This paper from the Royal Bath Hospital, Harrogate, Yorks, records another satisfactory experience with the simple slide test utilizing the commercial preparation of latex particles coated with a globulin for the diagnosis of rheumatism. The results, which were read macroscopically at one minute, were compared with those of the differential agglutination (D.A.) test. Of 603 sera examined, 232 gave a positive result by the latex slide (L.S.) test, and of these only 4 failed to give a positive D.A. reaction, which is defined as a differential titre of 1:16 or greater. No serum giving a positive D.A. reaction failed to give a positive L.S. test result. After clinical classification 85% of those classified as "definite or probable" rheumatoid arthritis gave positive L.S. test results, while of those classified as "possible" rheumatoid arthritis, 44% did so. The incidence of false positive reactions was assessed at 3·8% in cases without any suggestion of rheumatoid arthritis and at 5·3% in those of osteoarthrosis. Only occasional positive reactions were obtained in the sera of patients with such conditions as ankylosing spondylitis, Still's disease, and psoriasis with arthritis. The percentage of positive results was lower in early cases, long-standing cases, and those in which the arthritis was "mild in extent". In relation to clinical activity of the disease 88% of those with active arthritis gave a positive result compared with 54% of those with inactive disease. No correlation was found between L.S. test results and disease activity as measured by the erythrocyte sedimentation rate or haemoglobin level, but positivity was related to the radiographic bone changes and the presence of nodules. The test is shown to be simple to perform, easy to read, and qualitatively as satisfactory as the more extensive and time-consuming erythrocyte agglutination methods.
Harry Coke

800. **The Combination of Prednisone with Phenylbutazone in the Treatment of Rheumatic Conditions.** (L'association fixe de prednisone et de phénylbutazone (G 31109) en pratique rhumatologique)
E. Meyer, F. Thevenoz, G. H. Fallet, and E. Martin. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **27**, 313–322, Sept. [received Nov.], 1960. 36 refs.

This paper from the University Medical Clinic, Geneva, reports the results of treatment of 250 cases of various types of "rheumatism" with tablets containing 50 mg. of phenylbutazone and 1·25 mg. of prednisone. Previous work on this combination of drugs is described. There was no control group, but the criteria of improvement were laid down before the start of treatment. By these, improvement occurred in from 50 to 75% of cases of osteoarthritis of the limbs, periarthritis of the shoulder, non-articular rheumatism, low back pain, and rheumatoid arthritis. On the other hand little benefit was obtained in sciatica and cervical osteoarthritis, especially the chronic forms of these. The average daily dose was between 2 and 6 tablets a day. Side-effects, which were minimal, included 3 cases of skin irritation, several of minor gastric upset, and one case of reactivated duodenal ulceration. It was found that some cases could be treated with these tablets for as long as 11 months.
G. S. Crockett

801. **Peptic Ulcer in Rheumatoid Arthritis and Relationship to Steroid Treatment**
R. Bowen Jr., J. G. Mayne, J. C. Cain, and L. G. Bartholomew. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **35**, 537–544, Sept. 14, 1960. 10 refs.

An investigation was carried out at the Mayo Clinic to determine the incidence of peptic ulceration in patients with rheumatoid arthritis and the effect, if any, which steroid therapy has on this incidence. A total of 2,114 patients in whom rheumatoid arthritis was diagnosed in the 2 years 1954 and 1957 were divided into two groups: (1) 1,237 patients who had received systemic steroid therapy; and (2) 877 who had not been given such treatment. In addition a number of patients in Group 1 who had clinical signs of hypercortisonism as a result of treatment were separately studied. The ages of the majority of the patients ranged from 40 to 69 years, but 49 patients were aged under 10 and 18 over 80. The authors note that in 1947—before steroids were available—23 (3·3%) of 830 patients with rheumatoid arthritis had peptic ulcer. In 1954, of 627 arthritics given steroids, 42 (6·7%)

had peptic ulcer compared with 34 (6·8%) of 501 not so treated. In 1957 the figures were 51 (8·4%) of 610 and 37 (9·8%) of 376 respectively. In the subgroup of 331 treated arthritics with hypercortisonism the incidence of peptic ulcer was 5·7% in 1954 and 9·9% in 1957. Of 93 steroid-treated patients with ulceration, 17 (18·3%) had a gastric ulcer, while of the 71 patients with ulceration not so treated, 5 (7%) had gastric ulcer. Of a group of 65 patients given intra-articular injections of steroids in 1954, 2 had peptic ulcer and of 44 so treated in 1957, 4 had peptic ulcer. In all 6 cases the ulcers had been present before treatment started and were not aggravated by it. Of the 1,237 patients treated with steroids, 14 had severe gastro-intestinal haemorrhage and 3 had perforation; of the 877 not so treated, 19 had haemorrhage but none had perforation.

The authors quote figures to show that the incidence of peptic ulcer in patients with rheumatoid arthritis seen at the Mayo Clinic and the Massachusetts General Hospital before the introduction of cortisone was 3·3 to 4·7%. In the general population of North America it has been reported to be 1 to 3% and in England 3·4% in males and 0·7% in females. They consider that the most significant finding in their investigation is the increase in the incidence of gastric ulcer—18% of the peptic ulcers in the steroid-treated patients being gastric as against 7% in those not so treated. Whether the increase in the incidence of peptic ulceration among arthritics from 3·3% in 1947 to 8% for the two years 1954 and 1957 combined is real or is due to better diagnosis cannot be decided.

William Hughes

LUPUS ERYTHEMATOSUS

802. **Familial Occurrence of Systemic Lupus Erythematosus**

A. A. MARLOW, H. D. PEABODY JR., and W. R. NICKEL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 1641–1643, Aug. 13, 1960. 11 refs.

From the Mercy and County Hospitals, San Diego, California, the authors report 4 well-documented cases of systemic lupus erythematosus (S.L.E.) occurring in 2 sisters of Italian ancestry and in a mother and her married daughter of Mexican origin. The 15 previously reported cases of S.L.E. showing a familial incidence are briefly reviewed. [The authors do not attempt to explain the relationship.]

R. E. Tunbridge

803. **Current Therapy of Systemic Lupus Erythematosus. A Comparative Evaluation of Corticosteroids and Their Side-effects with Emphasis on Fifty Patients Treated with Dexamethasone**

E. L. DUBOIS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **173**, 1633–1640, Aug. 13, 1960. 18 refs.

In the first part of this paper from the University of Southern California School of Medicine, Los Angeles, the author presents an excellent summary of his personal clinical experience of 400 cases of systemic lupus erythematosus (S.L.E.) and of the principles he has applied in therapy. [But the majority of rheumatologists and others unfamiliar with the author's previous writings will hesitate to accept his opening sentence stating that "systemic lupus erythematosus . . . is a malignant variant of rheumatoid arthritis".] The second half of the paper records the results of the treatment with dexamethasone (9α-fluoro-16α-methylprednisolone) of 50 patients suffering from S.L.E. and compares the side-effects observed in this series with those in previous series treated respectively with methylprednisolone (40 cases), triamcinolone (29), and prednisone and prednisolone (37). [The method of sequential comparison adopted by the author is unacceptable to many authorities as a valid basis for comparison. Further, the period of treatment varied from one to 15 months and the steroid therapy was supplementary to other forms of treatment; thus 24 patients received salicylates to the point of mild toxicity and 17 were taking antimalarial drugs. Again, 29 patients received dexamethasone as their initial steroid therapy, but 21 were transferred to this drug from treatment with other steroids. Also reference is made to one of the author's series in which 38·7% of the patients exhibited spontaneous improvement before steroid therapy was even begun. Lastly, no detailed analysis of the severity or of the duration of the disease before steroid treatment was started in these 50 cases is given.]

The dosage of dexamethasone varied from 1 to 6 mg. daily, usually divided in two doses, but in 2 critically ill patients a dosage of 24 mg. daily was employed for 2 to 3 weeks. The pattern of clinical improvement with dexamethasone paralleled that in previous series in which other steroids were used. However, a higher percentage of dexamethasone-treated patients (especially those initially treated with the drug) exhibited Cushingoid features, more insomnia, and a greater degree of pitting oedema—28% compared with a mean of 3·6% for the other steroid preparations. In a special study of the incidence of peptic ulcer 14 patients underwent baseline radiographic studies before the start of dexamethasone therapy and these, together with 13 others, were examined radiographically at varying intervals thereafter. [It is difficult from the information provided to understand the rationale for selecting the patients or deciding the time intervals between the radiographs.] This study revealed 6 new peptic ulcers after periods of therapy ranging from 2 to 18 months, all of which were symptomatic. In all, 11 patients receiving dexamethasone had epigastric discomfort, 5 had a demonstrable ulcer, and one had a haematemesis, although three preceding radiographs had been normal. The author concludes that the incidence of peptic ulcer after dexamethasone therapy is no greater than after treatment with prednisone, methylprednisolone, or triamcinolone. There is a suggestion that the incidence of ulcer is greater when the patient is receiving a larger dosage of the steroid.

The final conclusion is that in the treatment of S.L.E. dexamethasone is as effective therapeutically as the other steroid preparations previously tried, but that it produces an appreciably higher incidence of side-effects, particularly pitting oedema and insomnia, and for this reason it is not to be preferred to other steroids.

R. E. Tunbridge

Neurology and Neurosurgery

804. **Craniostenosis.** (Краниостеноз)
V. A. KOZYREV. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 1115–1119, No. 9, 1960. 1 fig., 17 refs.

Craniostenosis as a nosological entity is comparatively rare, Günther having estimated its incidence at one per 1,000 births. The present report is based on the study of 63 cases referred to the Burdenko Neurosurgical Institute, Moscow, for operation between 1945 and 1958, 40 of the patients being male and 23 female [but only 60 are considered in the discussion]. The patients' ages ranged from 2 to 35 years. Craniostenosis was present at birth in 3 cases and developed at varying periods after birth in 57. It has been attributed by some authorities to inflammatory processes in the meninges or cranial bones, by others to birth trauma, rickets, endocrine disturbances, or abnormal metabolism, while in some instances heredity has been invoked. The author considers that it is due to faults in the laying down and evolution of bone in the embryo.

The cases are classified according to the sutures involved. Mental retardation occurs earliest in patients in whom all the sutures are affected.

The cardinal signs are those of increased intracranial pressure (acute attacks of headache with vomiting), changes in the optic fundi (choked disks and secondary optic atrophy), exophthalmos (47 cases), psychological symptoms (18), epileptiform convulsions (15), meningeal symptoms (20), cranial nerve palsies, especially of the 6th nerve, and tonic or clonic nystagmus (16 cases). Craniograms showed absence of one or more sutures, and pneumoencephalograms revealed evidence of compression of the brain. The cerebrospinal fluid was usually normal. The results of operation were on the whole favourable; 34 children were able to attend school (only 8 had to go to special schools for poor sight), 7 went on to higher educational centres, while adults were able to resume work.

[No details of the operative procedure are given.]

L. Firman-Edwards

805. **Amyotrophic Lateral Sclerosis: a Clinical Study of 50 Cases from the Viewpoint of External Factors of Causation.** (Боковой амиотрофический склероз. Клиническое исследование 50 больных с точки зрения влияний внешней среды)
M. ŠERCL' and JA. KOVARŽIK. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **60**, 1101–1105, No. 9, 1960. 1 fig.

The authors have studied 50 cases of amyotrophic lateral sclerosis from the aetiological aspect. The sex incidence was equal and the age range from 31 to 69 for the men and 23 to 66 for the women. In 23 cases the first symptoms appeared in the lower extremities, in 16 in the upper extremities, and in 11 in the brain-stem. Of the 29 patients who died, 23 lived for 3 to 5 years after onset of the disease, 2 for over 5 years, and 3 under 2 years; in one case the time of onset could not be determined. In regard to nature of employment, 41 of the patients were engaged in physical work, 8 in mental work, and in one case the occupation was undetermined; over half lived in a rural environment.

In 30% of cases onset of the disease was associated with an infectious disease, 22% had a history of severe disorder of the alimentary tract such as chronic gastritis, gastric ulcer, chronic cholecystitis, and traumatic injury to the liver, while 10% gave a history of recent heavy physical strain. Although such circumstances could have had some effect in precipitating the disease, the authors consider that any aetiological relationship is obscure and doubtful. Over two-thirds of the patients lived at an altitude of 200 to 400 metres (650 to 1,300 ft.) above sea level, and 16% at between 400 and 500 metres, only one patient living below 200 metres [but in a mountainous country such as Czechoslovakia (from which the report comes) this is surely not unusual]. Nearly 80% lived on alluvial or diluvial soils, that is, gravel and sand over chalk, and 16% on other types of subsoil. In the whole series only one patient could be said to show definite evidence of a familial factor, though in 4 others there was some indication of this. In no case was there evidence of radioactivity in the environment. The aetiology of this disease thus remains obscure, and treatment completely inefficacious.

L. Firman-Edwards

806. **The Surgical Treatment of Parkinsonism**
F. J. GILLINGHAM, W. S. WATSON, A. A. DONALDSON, and J. A. L. NAUGHTON. *British Medical Journal* [*Brit. med. J.*] **2**, 1395–1402, Nov. 12, 1960. 7 figs., 17 refs.

The authors report from the University of Edinburgh the effect of producing electrocoagulation lesions in the globus pallidus, internal capsule, and thalamus, separately or in combination, in an unselected group of 60 patients with Parkinsonism operated on during the 5 years 1955–60. All except one of the patients were under 65. The choice of site for the operative lesion was modified as experience accumulated. In the earlier cases the lesion was made in the globus pallidus, but in nearly one-third of them an additional lesion was made in the ipsilateral thalamus to control tremor. In the second phase the lesion was sited in the thalamus initially, but rigidity was not resolved as completely as with a lesion in the globus pallidus. The present practice, which is to make an initial double lesion in the thalamus and globus pallidus, in each case close to the internal capsule, appears to produce the best results in controlling both tremor and rigidity.

In only one patient of the series have limb tremor and rigidity remained unimproved. Complications after the operation persisted in 6 patients who were successfully

treated for tremor and/or rigidity, and several interesting temporary complications, such as transient dysphasia, were encountered. In one patient with moderately severe diabetes mellitus control was maintained with one-half the previous dosage of insulin after successful operation for Parkinsonism. There were no immediate postoperative deaths, but one patient died after many months of stupor resulting from a ventricular haemorrhage.

[It is perhaps a pity that in this interesting study there is no indication of the aetiological factors concerned in the pathogenesis of Parkinsonism in individual patients.] *J. B. Stanton*

807. **Treatment of Multiple Sclerosis with Tolbutamide**
G. T. SAWYER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **174**, 470–473, Oct. 1, 1960. 6 refs.

The author of this paper from the University of Minnesota Medical School and the Veterans Administration Hospital, Minneapolis, describes a trial of tolbutamide in the treatment of disseminated sclerosis. The drug was given to 7 patients, aged 22 to 46 years, in a dosage of 0·5 to 1·5 g. daily, alternating in 6 of the patients with a placebo. Improvement was stated to occur 2 to 7 days after the start of tolbutamide therapy when a low-carbohydrate diabetic diet (2,000 Calories) was taken. Deterioration was observed when the placebo was substituted for tolbutamide and when a high-carbohydrate diet was given. *I. Ansell*

BRAIN AND MENINGES

808. **A Humoral Agent Implicated in Vascular Headache of the Migraine Type**
L. F. CHAPMAN, A. O. RAMOS, H. GOODELL, G. SILVERMAN, and H. G. WOLFF. *Archives of Neurology* [*Arch. Neurol.*] **3**, 223–229, Sept., 1960. 10 figs., 15 refs.

Attacks of migraine are characterized by dilatation of the large and small vessels of the head, both intracranial and extracranial; yet similar dilatation of these vessels by, for example, immersion of the body in hot water does not produce the headache or other symptoms of migraine. Previous workers have isolated a pain-producing substance from blister fluid which had many of the properties of the vasodilator polypeptides. The present authors, working at New York Hospital–Cornell Medical Center, have sought to isolate a similar substance from specimens of subsurface tissue fluid collected from patients with headache.

Bio-assay studies showed that this fluid contained a substance which relaxed isolated rat duodenum, contracted rat uterus, and lowered the rat's blood pressure. A constant ratio of activity among several specimens indicated that the observed activity was due to a single substance, which could be distinguished from serotonin, potassium, adenosine triphosphate, substance P, acetylcholine, and histamine. The substance became less active on standing, boiling with alcohol stabilized it, while incubation with chymotrypsin inactivated it, indicating that the active substance remaining after stabilization is a polypeptide. This substance, which is similar to bradykinin and " plasma kinin " and for which the authors propose the name " neurokinin ", occurs in the cerebrospinal fluid during severe and prolonged attacks of headache of migrainous type. The amount of neurokinin in the subsurface fluid of the heads of patients during headache averaged 8 times (and in rare instances as high as 35 times) as much as control values, the amount being closely related to the severity of the attack. Administration of ergotamine tartrate reduced the migrainous features of an attack and also the polypeptide content of the subcutaneous fluid.

It is suggested that possibly during such headache this fluid contains a proteolytic enzyme capable of cleaving plasma globulin to form neurokinin, and that the action of ergotamine tartrate may partly depend on its interference with the action of protease and polypeptide. Attacks of migraine are often associated with activity of the central nervous system, since they occur after long periods of alertness, striving, extraordinary effort, or major frustration. The painful local reaction may be an epiphenomenon of excessive operation of the normal mechanism for functional vasodilatation within the central nervous system. " The result is a sterile inflammatory reaction, neurogenically induced."
A. C. F. Green

809. **Pathways of Cerebral Collateral Circulation**
M. TATELMAN. *Radiology* [*Radiology*] **75**, 349–362, Sept., 1960. 20 figs., 37 refs.

Pointing out that despite considerable anatomical proof to the contrary the myth of " end-artery " circulation in the brain has been perpetuated in textbooks for years, the author presents from Wayne State University College of Medicine, Detroit, an evaluation of the incidence of cerebral collateral circulation based on angiographic studies in over 700 patients with the stroke syndrome. The demonstration by Kramer as early as 1912 that in normal conditions each internal carotid artery supplies blood only to the distribution of its anterior and middle cerebral arteries and each vertebral artery, via the basilar, only to the distribution of the cerebellar and posterior cerebral branches is amply borne out by everyday experience with normal internal carotid and vertebral angiograms. Thus, the author continues, " it is seen that the circle of Willis acts as a shunt mechanism and does not, under normal circumstances, allow mixing of blood coming from each of the two internal carotid arteries and the basilar artery ".

Collateral cerebral blood flow, that is, reversal of the normal direction of flow, may be caused by any process which narrows or dilates the lumen of a vessel, either peripherally or centrally, and the numerous conditions in which this has been demonstrated angiographically are tabulated. A collateral circulation was observed in 61·7% of 191 cases of complete or partial occlusion of the cerebral vessels. The range for various sites of occlusive disease was from 10·5 to 84·6%, with 60% or over for most sites and in the region of 80% for many. The author suggests that these percentages would probably be higher if vertebral as well as bilateral carotid arterio-

graphy had been carried out in every case. He notes that collateral circulation rarely occurs in normal persons and if such communication is found on angiography a search should be made for its cause. If such cause is not to be found in the internal carotid or basilar arteries then complete examination of the vertebral and carotid arteries, particularly at their points of origin, must be made.

[This paper presents an interesting evaluation of the evidence of collateral intracranial circulation as revealed by angiography and should be read in full.]

J. MacD. Holmes

810. **Vascular Lesions of the Visual Cortex with Brain Herniation through the Tentorial Incisura: Neuro-ophthalmologic Considerations**

W. F. HOYT. *Archives of Ophthalmology* [*Arch. Ophthal. (Chicago)*] **64**, 44–57, July, 1960. 8 figs., 20 refs.

It is generally recognized that infarction of the occipital lobes may occur in patients with expanding supratentorial lesions or rapid swelling of the brain, being a result of a shift of the brain downward through the tentorial opening with consequent compression of the posterior cerebral arteries against the edge of the tentorium. During the acute phase of pressure patients with tentorial herniation may show homonymous field defects as sequelae of the arterial compression.

Proof that these patients have suffered tentorial herniation and compression of a posterior cerebral artery is difficult, but certain factors in the history that increase the likelihood that this has occurred are a history of a period of severe increased intracranial pressure with papilloedema, with or without unconsciousness, and rapid development of homonymous hemianopia during the phase of increased pressure. Other suggestive evidence is the finding of partial ptosis or unilateral dilatation of the pupil, rapid deterioration of the state of consciousness before remedial surgical treatment, and the history of a spinal tap or performance of pneumoencephalography on patients with signs of increased intracranial pressure. Hemianopia due to ischaemia of the visual cortex develops rapidly and tends to be total. When the hemianopia is relative the Riddoch phenomenon—in which a moving test object may be perceived but a stationary test object remains imperceptible—may be quite striking. Patients who have suffered tentorial herniation (secondary to pressure, trauma, bleeding, or tumour) may recover, so that the visual fields show wide macular sparing and eventually full peripheral recovery.

S. J. H. Miller

811. **Subacute Encephalitis of Later Adult Life Mainly Affecting the Limbic Areas**

J. B. BRIERLEY, J. A. N. CORSELLIS, R. HIERONS, and S. NEVIN. *Brain* [*Brain*] **83**, 357–368, Sept., 1960. 11 figs., 6 refs.

In this paper from the Maudsley and King's College Hospitals, London, and Runwell Hospital, Essex, the authors describe the clinical features and post-mortem findings in 3 cases of subacute encephalitis occurring in men aged 53, 56, and 58 respectively. The first patient presented with a depressive illness and bizarre behaviour disorder, the second had signs resembling general paralysis of the insane, and the third presented with shoulder girdle pain and later tiredness and depression; a common feature in all was a progressive dementia. The authors remark that none of the cases had the characteristics, namely, abnormal movements and myoclonus, of the subacute encephalitis of Dawson and van Bogaert. Syphilis was carefully excluded in all 3 cases.

Although these cases formed a heterogeneous group the necropsy findings and especially the histological examination results confirmed that in all 3 there was an encephalitic process, the brunt of which was borne by the "limbic" lobes. The "limbic" areas are defined as that part of the brain including the uncus, amygdaloid nucleus, hippocampus, and the dentate, hippocampal, and cingulate gyri, together with the limen insulae. In these areas there was evidence of inflammatory reaction, but none of haemorrhage or necrosis; the inflammation was confined almost entirely to the grey matter and no inclusion bodies could be demonstrated. The authors contrast this last finding with the reported cases of post-herpetic encephalitis, in which inclusion bodies are almost a constant finding, and with other reported cases in which, although there were no demonstrable inclusion bodies, the onset and course of the illness was acute. They make the tentative suggestion that the 3 cases described form a distinct group of subacute encephalitis in which the temporal lobes are selectively involved and in which a viral aetiology is most likely.

Although [unfortunately] no post-mortem viral studies were carried out, extensive ante-mortem viral studies were performed in one of the cases and gave negative results.

J. B. Foster

812. **A Review of the Literature on the Relationship of Epilepsy and Intelligence in Schoolchildren**

L. E. KEATING. *Journal of Mental Science* [*J. ment. Sci.*] **106**, 1042–1059, July [received Oct.], 1960. Bibliography.

This review of the literature on intelligence in epileptic children includes data on the I.Q. of such children, the association of epilepsy with mental deficiency (both oligophrenic and associated with gross cerebral lesions), mental deterioration in epileptic children, the effect of seizures on the brain, hereditary factors in epilepsy associated with mental deficiency, the influence of anticonvulsant drugs on performance in intelligence tests, and the electroencephalographic patterns in association with mental deterioration. The author states that although there is little evidence in the literature that in general intelligence is lower in epileptics than in non-epileptics, certain groups of epileptics "reveal mental shortcomings and in some cases progressive deterioration." It is suggested that further research should be directed to these groups and to the qualitative aspects of the association between epilepsy and mental deficiency. The effects of anticonvulsant drugs should be studied in relation to individual mental processes rather than to general intelligence level.

[The bibliography contains some 160 titles.]

J. B. Stanton

Psychiatry

813. **Physical Disorders in Psychiatric Illness: a Study of 209 Consecutive Admissions**
C. F. HERRIDGE. *Lancet* [*Lancet*] **2**, 949–951, Oct. 29, 1960. 6 refs.

A study of the prevalence of physical disorders in psychiatric patients was carried out at Atkinson Morley's Hospital, London, it being considered that in theory organic illnesses may prove to be causal, contributory, consecutive, or coincidental with respect to psychiatric symptomatology. During an 8-month period 209 patients (100 men and 109 women) admitted consecutively to the 44-bed psychiatric department were investigated with regard to the presence of physical as well as psychiatric disorder. The psychiatric diagnosis showed a preponderance of cases of endogenous and reactive depression and schizophrenic disorders.

It was found that in 11 cases (5%) physical disease constituted the major diagnosis, despite the fact that the cases had been labelled "functional" on admission. Among this group there were 4 cases of intracranial disease (for example, primary or secondary neoplasm) and 7 of extracranial disease (for example, bronchial carcinoma, uraemia, or pulmonary tuberculosis). Details of a number of cases are provided.

In 43 cases (21%) there was some physical disorder (for example, head injury, epilepsy, hypertension) which was considered to be contributory to the psychiatric state. In 15 cases (7%) a physical disorder evidently resulted from the psychiatric illness or its treatment, and this group included 3 cases of phlebothrombosis as a complication of phenelzine therapy. In 34 cases (16%) there were physical disorders (for example, pulmonary tuberculosis, dental conditions, mitral valvular disease) which were considered to be coincidental with the psychiatric illness.

It is concluded that psychiatrists need to adopt a global viewpoint in the appraisal of their patients' illnesses. Medical disorders may sometimes masquerade as psychiatric syndromes. *A. Balfour Sclare*

814. **A Method of Creating Aversion to Alcohol by Reflex Conditioning in a Group Setting**
E. C. MILLER, B. A. DVORAK, and D. W. TURNER. *Quarterly Journal of Studies on Alcohol* [*Quart. J. Stud. Alcohol*] **21**, 424–431, Sept. [received Nov.], 1960. 17 refs.

An experiment to test the practicability of aversion therapy of alcoholics carried out in a group setting is reported from Tulane University School of Medicine, New Orleans, Louisiana. In their methodology the authors followed the basic principles of conditioned reflex therapy for alcoholism as introduced by Voegtlin (*Amer. J. med. Sci.*, 1940, **199**, 802), special attention being paid to minimizing external stimuli and to timing administration of alcohol during treatment sessions. Care was taken to ensure that no patient suffered from psychosis or from any physical disability that would preclude such therapy. The 20 patients included in the investigation were white males who admitted that they had a drinking problem and wanted to stop the habit. The medication used was a mixture of emetine, pilocarpine, and ephedrine; no adjuvant psychotherapy was given. Patients were treated in groups of 4 in a special room. Treatment lasted for 2 weeks, being given every day except Saturdays and Sundays—that is, 10 treatment sessions in all. All 20 patients are stated to have acquired "excellent conditioned aversion to all forms of alcohol which were presented to them". After 8 months, of 10 patients whose follow-up was adequate, only 2 had reverted to their former pattern of drinking.

The authors discuss the theoretical problems of their technique of group conditioning as distinct from the established method of individual aversion therapy.

[Although the sample is small, clinical details are not given, and the follow-up is short, nevertheless the experiment is interesting and merits further research. If found successful it will certainly make aversion therapy much more economical.] *N. H. Rathod*

815. **The Place of Iproniazid in the Treatment of Depressive States.** (Place de l'iproniazide dans le traitement des états dépressifs)
J. M. SUTTER, Y. PELICIER, and G. PASCALIS. *Annales médico-psychologiques* [*Ann. méd.-psychol.*] **118**, 447–454, Oct., 1960.

The results of treating 15 depressed patients with iproniazid are considered in respect of three groups: (1) 4 patients who received iproniazid only; (2) 8 to whom iproniazid was given together with either vibration therapy or imipramine; and (3) 3 patients who received iproniazid and later developed hypomanic or manic symptoms. In addition to these drugs the patients were given a hypnotic or chlorpromazine at night. A brief case history of each patient is presented.

Of the 15 patients, a favourable outcome was obtained in 12, the remaining 3 failing to respond to any therapeutic measure. Iproniazid had a definite therapeutic effect in 4 cases (including 2 patients who were being treated simultaneously for alcoholism) and a marked contributory role in another 8. It restored normal sleep in one patient in whom insomnia had been a serious problem, while in a further 4 patients iproniazid dramatically completed the recovery begun by electric convulsion therapy and imipramine. No particular type of depression seemed more likely than any other to respond to iproniazid, the dosage of which was usually 100 mg. per day in doses of 50 mg. morning and midday, with occasionally a third dose in the evening. The authors stress that because of the narrow margin between therapeutic and toxic doses close super-

vision is necessary. Only minor side-effects, such as headache and weakness, were noted and these occurred early in the treatment. The only notable complication was the development of hypomania in 3 patients in whom, however, reduction of the dose succeeded in restoring a more normal mood. *J. S. Bearcroft*

816. **" Tofranil " in the Treatment of Depressive States.** (Erfahrungen mit Tofranil in der Behandlung depressiver Zustandsbilder)
L. ANGYAL. *Wiener medizinische Wochenschrift* [*Wien. med. Wschr.*] **110,** 781–790, Sept. 24, 1960. 26 refs.

The author reports from the Metropolitan Hospital, Budapest, the results of treatment with " tofranil " (imipramine) of 82 patients (70 female), most of whom (67) were in-patients; the age range was from 24 to 75 (average 50·6) years. Treatment was started with 3 intramuscular injections of one ampoule daily [exact dose not stated] and increased to 3 injections of two ampoules daily. After 6 to 12 days the injections were gradually replaced by tablets, the number of which was reduced until a maintenance dose was reached, in most cases this being 2 tablets three times a day or 3 tablets in the morning and 2 at noon. To avoid causing insomnia the last dose was never given later than 5 p.m. The first effect of treatment was sometimes noted after 4 to 6 days, but generally not until after 10 to 14 days. Among the 31 patients with endogenous depression the improvement rate was 84% (26 cases), in the 24 with reactive depression it was 75% (18 cases), and in 9 with involutional depression it was 56% (5 cases). Schizophrenic patients showed no improvement.

No clinical contraindication to imipramine was observed. Liver function test results remained normal, as did also blood counts, though there was a slight increase in eosinophil granulocytes in almost half the patients. In the early stages of treatment rest in bed was prescribed, especially in elderly patients. The danger of suicide had to be guarded against in the 21 out-patients when improvement began to set in and removed the safeguard of motor retardation. One such patient in the series did commit suicide. Among the side-effects of the drug were palpitation, increased perspiration or dry skin, dry mouth, poor visual accommodation, constipation, drowsiness, weakness, dizziness, hand tremor, and occasionally a reduction in facial expressiveness. In a few cases sleeplessness had to be treated with sedatives. In 2 patients there was an initial retention of urine requiring catheterization, but this cleared up spontaneously, while in some cases hypomanic features occurred. None of these side-effects, however, were ever severe enough to necessitate a reduction in the dosage. *F. K. Taylor*

817. **A Psychological Analysis of Apparent Depression following Rauwolfia Therapy**
S. BERNSTEIN and M. R. KAUFMAN. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **27,** 525–530, Sept.–Oct., 1960. 15 refs.

Because reports of depression following administration of rauwolfia preparations have limited their full use the authors sought to establish objective criteria that would predict its occurrence. To this end 50 consecutive patients, 26 from the hypertensive and 24 from the dermatological clinics of the Mount Sinai Hospital, New York, were studied. The 26 men and 24 women, mostly middle-aged, were of low socio-economic status, 40% being of Puerto Rican or negro origin. The duration of illness was about 6 months in the hypertensive group and 3 to 5 years in the dermatological group.

Before receiving rauwolfia all patients had multiple base-line assessments, using the Funkenstein, Bellevue-Wechsler, and projective tests and a psychiatric interview. The Funkenstein and some of the psychological tests were repeated several times during the study. Psychologists and the psychiatrist independently rated each patient's depressive potential as high, moderate, or low, using as predictive criteria indications of: (*a*) previous depressions; (*b*) disturbed mood, psychomotor activity, or intellectual functioning; (*c*) chronic guilt associated with unfulfilled hopes or obligations; (*d*) intensive ambivalence to and strong dependence on a love object; (*e*) a sense of total social rejection; and (*f*) frustration or despair in face of shrinking personal horizons. Patients in Funkenstein's Group VI or VII were weighted toward the " depressive vulnerable " group.

Of the 50 patients, 47 received " raudixin ", 50 to 400 mg. daily by mouth; the other 3 had oral " serpasil ", 1 to 5 mg. daily. All were followed up for 12 to 18 months while taking the drugs. Unfortunately for the aims of the investigation, during this period not a single case of true depression occurred. However, 12 patients responded with " pseudo-depression ", a reaction of excessive tranquillization in which the principal complaints were of being slowed and tired. Of these 12 patients, 11 were from the hypertensive group, and this reaction is related to their psychodynamic make-up, as inferred from the initial examination. The hypertensive patients were characterized by obsessive character traits; in 14 excess psychomotor activity was considered to be an important defence reaction, and it was amongst these that the 11 " pseudo-depressions " occurred. While appreciating the limitations of the study, the authors postulate that pharmacological reduction of psychomotor activity threatens those patients for whom such behaviour is a defence against fears of inadequacy.

By contrast with the hypertensive group, patients with skin disorders were characterized by timidity and passivity; anxiety rather than anger was the predominant affect, and psychomotor activity was rarely used as a defensive manœuvre.

The Funkenstein test showed that patients were almost equally distributed among the 7 groups, and although shifts did occur during treatment, no correlation with change of symptomatology was found.

It is felt that the findings raise the question of whether the relation of depression to treatment with rauwolfia drugs may not be coincidental rather than causal.
Alan A. Black

818. **Late Results of Orbital Undercutting: Report of 76 Patients Undergoing Quantitative Selective Lobotomies**
W. B. SCOVILLE. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **117,** 525–532, Dec., 1960. 3 figs., 24 refs.

Dermatology

819. **Cutaneous Manifestations of Systemic Disease**
R. R. KIERLAND. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **35**, 451–459, Aug. 3, 1960.

A large number of cutaneous manifestations of systemic disease are grouped and discussed according to such underlying conditions as pruritus, peripheral vascular disease, pigmentary disorders, anaemia and purpura, and amyloidosis. The skin changes are not described in detail, but attention is drawn to some of the more significant features. While for the most part the common affections are discussed, a number of more rare disorders are mentioned, such as the pigmentation in Albright's syndrome, necrobiosis lipoidica, and the Peutz–Jegher syndrome.

[This is a useful though not complete review for reference. Pruritus may arise from arteriosclerosis in the aged and acneform eruptions are seen on the face in polycythaemia. Xanthomata are observed in myxoedema, portal cirrhosis, and nephrosis as well as in diabetes.] The author states that the skin conditions manifest in the collagen disorders were omitted " because of lack of space ". *John T. Ingram*

820. **Some Dermatological Hazards of To-day**
F. R. BETTLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 1467–1473, Nov. 19, 1960. 31 refs.

821. **Triclobisonium Chloride and Triclobisonium–Hydrocortisone Ointments in Dermatologic Therapy**
J. A. HUNT and B. M. JAMES. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **7**, 477–480, Aug., 1960. 9 refs.

The authors consider there is a need for new and better antibacterial agents in the treatment of primary skin infections and secondarily infected dermatoses. In this paper from St. Michael's Hospital, Newark, and Orange Memorial Hospital, New Jersey, they report a study of the efficacy of 0·1% triclobisonium chloride (a derivative of 1:6-hexanediamine) in a carbowax base and, in steroid-responsive dermatoses secondarily infected, of this ointment with 0·5% hydrocortisone. The patients were selected from routine hospital admissions and from private practice, a total of 249 with proved infections, as determined by the results of culture, being included. *Staphylococcus aureus*, coagulase positive or negative, was isolated in 80% of the cases, a combination of two or more bacteria being isolated in 30%. No antibiotics were given.

Primary skin infections, which were present in 113 patients, included impetigo, paronychia, folliculitis, furunculosis, and sycosis vulgaris. Following treatment with triclobisonium chloride 99 patients (88%) were considered to be cured, 4 were improved, and 7 unimproved. There was objective evidence of a flare-up in one patient, and a patch test with the ointment gave a positive reaction; in the remaining 2 patients subjective symptoms such as irritation and increased itching occurred, but the results of patch tests were negative. There were no recurrences in this group.

Of 136 patients with secondarily infected dermatoses (including contact dermatitis, atopic dermatitis, tinea pedis, chronic eczema, and seborrhoeic dermatitis) treated by application of triclobisonium ointment with hydrocortisone, 96 (71%) were considered to be cured, 21 to be improved, and 13 unimproved. Adverse reactions occurred in 6 patients, the results of patch tests being positive in 3. *P. T. Main*

822. **Topical Triamcinolone in Eczema**
C. F. H. VICKERS and S. M. TIGHE. *British Journal of Dermatology* [*Brit. J. Derm.*] **72**, 352–354, Oct., 1960.

The results are presented of a double blind paired comparative trial of ointments containing 1% hydrocortisone and 0·1% triamcinolone acetonide. The latter is shown to exert a more powerful and more rapid anti-inflammatory effect in patients with various forms of eczema.—[Authors' summary.]

823. **Treatment of Urticaria and Quincke's Oedema with a Synthetic Antimalarial Drug: Amodiaquine**
E. SIDI and A. REINBERG. *Lancet* [*Lancet*] **2**, 842–843, Oct. 15, 1960. 10 refs.

Following a chance observation of the value of the antimalarial drug amodiaquine in controlling chronic urticaria the authors investigated further its previously reported anti-allergic effect. They now publish their results in 22 cases of intractable urticaria treated with amodiaquine at the Fondation A. de Rothschild, Paris. In some of the cases there was an associated Quincke's oedema. In 12 cases the drug was given alone in a dosage of 200 to 400 mg. daily for the first week and then 200 or 100 mg. daily during subsequent weeks. Treatment was interrupted after 4 weeks or continued in low dosage (100 to 200 mg. weekly). Results are described as " excellent " in 4 cases, " good " in 4 cases, and " no response " in 4 cases. In the other 10 cases amodiaquine was combined with an antihistamine drug (7 cases) or with antibiotics (3 cases). In this group there were 6 successful results and 4 failures. In 2 of the successful cases the drug had to be discontinued because of side-effects—namely, nausea, vomiting, and diarrhoea.

[In treating a condition which may fluctuate in severity or may resolve itself spontaneously, and which may be subject to suggestion, it is difficult to discount the element of chance in producing good results. However, to obtain a favourable therapeutic effect in even 14 of 22 patients with an intractable condition is noteworthy and merits further controlled investigation.]
Benjamin Schwartz

Paediatrics

824. **On the Mechanism of Action of Vitamin B_{12} in Chronic Disturbances of Nutrition in Children.** (К вопросу о механизме действия витамина B_{12} при хронических расстройствах питания у детей)
G. A. MAKAROVA. *Вопросы Охраны Материнства и Детства* [*Vop. Ohrany Materin. Dets.*] **5**, 26–30, Sept.–Oct., 1960. 22 refs.

One of the most important metabolic effects of vitamin B_{12} is its ability to restore the S-S- and SH- groups which enter into the structure of numerous enzymes and play an essential part in the metabolism of the three basic foodstuffs. The vitamin was used in the treatment of 20 children aged 5 to 18 months suffering from underdevelopment of nutritional and infective aetiology, this therapy being preceded when necessary by specific treatment and/or blood transfusions. Laboratory investigations included blood examinations and determination of the blood glutathione level by the Balakhovskii cadmium method, for which only 0·1 ml. of blood is required. The vitamin was given intramuscularly and it was found that 15 μg. on alternate days, up to a total of 150 to 180 μg., was the optimum dose for children under 2 years of age. The blood glutathione level as determined in healthy adults and children ranged from 27·6 to 35·8 mg. per 100 ml., whereas in the infants with chronic nutritional disturbances the range was 15·05 to 26·6 mg. per 100 ml.

Treatment with the vitamin brought about improvement of appetite in all patients, this being associated with improvement in the general condition and in activity, and better sleep. Of the 20 patients, 16 showed a daily weight gain of 26 to 68 g. In the remaining 4, aged 11 to 17 months, daily weight increase was only 7, 14, 17, and 20 g. respectively, but these patients had previously shown the poorest weight gain. Determination of the blood glutathione level after treatment in 17 children showed in 12 an average increase of 3·6 mg. per 100 ml., normal values being reached in 5 of these. The increase in level was slight in 2 patients and 3 failed to show any increase, although 2 of the latter were still gaining weight at the rate of 40 and 32 g. respectively per day. Generally speaking the infants who showed the greatest increase in the blood glutathione level also showed the best weight gain. There was no definite relationship between the dose of the vitamin and the blood glutathione concentration.

The blood examinations confirmed the favourable effect of vitamin B_{12} on the blood picture and haemoglobin value.

S. W. Waydenfeld

825. **Meconium Ileus: an Eleven-year Review at the Hospital for Sick Children, Toronto**
J. A. MACDONALD and G. A. TRUSLER. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **83**, 881–885, Oct. 22, 1960. 3 figs., 18 refs.

826. **Carrot Broth in the Treatment of Toxic Dyspepsia in Infants.** (К вопросу о применении морковной диеты при лечении токсической диспепсии)
T. N. SUKOVATYH. *Вопросы Охраны Материнства и Детства* [*Vop. Ohrany Materin. Dets.*] **5**, 12–17, Sept.–Oct., 1960.

The advantages of the vegetable broth diet compared with the usual starvation and tea regimen as an adjuvant to the specific treatment of toxic dyspepsia in infants have been pointed out by previous workers. Of the vegetables suitable for this purpose, carrot is cheap and readily available, and its high content of minerals, especially of potassium salts, and pectins makes it particularly suitable. In the present study strained carrot broth enriched with sugar and lemon juice or ascorbic acid and providing 45 Cal. per 100 ml. was taken readily by the young patients, and was given as the only nourishment in quantities of 50 to 200 ml. per kg. body weight daily to 79 infants of various ages with toxic dyspepsia until vomiting stopped and the stools became normal in consistency. Most of the patients were admitted to hospital within 5 days of onset of the disease. A group of 21 similar children who received only a tea and glucose diet served as controls. All the patients were treated with antibiotics and infusions of glucose saline, with ascorbic acid as necessary.

The stools became normal within 3 days in a great majority of the infants given the carrot-broth diet compared with only 2 in the control group, and their stay in hospital was shorter in spite of the fact that on the average they were more seriously ill on admission. This group also showed less weight loss in the early stages of the illness and began to gain weight as early as the 2nd or 3rd day of treatment. Similar improvement was not, however, obtained in 5 infants admitted with 3rd-degree toxaemia, one of whom died. The author gives the warning that the carrot-broth diet should be used cautiously in infants with thrush or other fungal infection, since it is a good medium for fungus growth.

S. W. Waydenfeld

827. **Soluble Proteins in the Stools of Infants with Chronic Dysentery.** (Растворимые белки в кале детей с хроническими расстройствами питания)
A. P. MAKAROVA. *Вопросы Охраны Материнства и Детства* [*Vop. Ohrany Materin. Dets.*] **5**, 31–36, Sept.–Oct., 1960. 3 figs., 21 refs.

A definite straight-line relationship has been demonstrated between the concentration of soluble proteins in the stools of breast-fed infants and the functional state of the digestive apparatus. The lower the level of activity of the pancreatic enzymes, the greater the amount of soluble proteins in the stools and vice versa. This has been confirmed in the present study by the simultaneous determination of the faecal soluble protein content and

the direct estimation of lipase, trypsin, and amylase activity in the duodenal juice, obtained by aspiration. (The values obtained for faecal soluble protein content were divided by the factor 6·25 to obtain the concentration of soluble protein nitrogen.)

In the investigation of 13 infants with dystrophy, of the 2nd degree in 9 cases and of the 3rd degree in 4, it was found that the ratio of soluble protein N to total N in the stool changed considerably in the same infant during treatment. With improvement and gain in weight the content of insoluble protein N diminished more rapidly than did that of soluble protein N, with a consequent slight relative increase in the percentage of soluble protein N, although the absolute amounts of the two fractions were reduced. At the same time the activity of the pancreatic enzymes generally increased; in only 2 patients did trypsin activity, in 4 amylase activity, and in 3 lipase activity fail to increase. It is concluded that the faecal soluble protein content is thus a good index of pancreatic function.

S. W. Waydenfeld

828. **The Diagnosis of Ebstein's Anomaly during Life.** (Zur Diagnose des Ebstein-Syndroms *intra vitam*)
H. Steim, C. S. So, and J. Emmrich. *Archiv für Kinderheilkunde* [*Arch. Kinderheilk.*] **162**, 252–280, 1960. 6 figs., bibliography.

The authors describe 8 cases of Ebstein's disease encountered among 1,000 patients examined by cardiac catheterization at the University Medical Clinic, Freiburg, since 1953. In 3 cases the post-mortem findings included: (1) a hypertrophied, dilated right auricle; (2) a congenitally deformed tricuspid valve with its anterior cusp arising from the fibrous ring and its medial and inferior cusps from the posterior ventricular wall or the ventricular septum; (3) a displacement of the valve into the right ventricle, the proximal portion of which was dilated and thin-walled so that with the right auricle it formed one large cavity; and (4) a small distal ventricle with normal walls. Heredity was not a factor of aetiological importance in any of the authors' cases, nor were foetal endocarditis, chromosomal causes, or maternal infections in early pregnancy. The clinical picture was diagnostically unhelpful. The most constant auscultatory sign was a left parasternal systolic murmur radiating to the apex. Phonocardiograms confirmed that the murmur was loudest in the 4th left intercostal space and at the apex; a diastolic murmur was never heard. In the electrocardiograms preponderance was to the right in 4 cases, to the left in 2, and equivocal in 2. Conspicuously widened P waves were present in 6 cases, and in 5 there was an abnormally wide QRS complex. Fluoroscopy showed a characteristically bag-shaped heart as a result of the enormous right auricle. Auricular pulsations were seen in the kymogram along the right lateral border and at the lower two-thirds of the left lateral border. Angiocardiography was not performed in view of the considerable dangers in the circumstances prevailing.

The authors stress that in this condition cardiac catheterization is the diagnostic method of choice, for with it a positive diagnosis was possible in every one of their cases, and they encountered no untoward complications, although the catheter tended to curl up in the huge auricle. Minor disturbances occurred when the catheter reached the valve. In 2 cases gross valvular deformity made it impossible to pass through the right ventricle into the pulmonary artery. The pressure levels in both the proximal and distal portions of the right ventricle must be determined to confirm the diagnosis. In all cases in which there was tricuspid incompetence the ventricular systolic wave was higher than the auricular contraction wave, and the mean auricular pressure was in all cases except one higher than normal. The mean pressure in the distal portion of the right ventricle was always much higher than that in the proximal portion. The degree of difference between the higher pressure in the proximal portion of the ventricle and the lower pressure in the right auricle allowed of assessment of the functional boundary dividing the two chambers. Blood gas analysis usually verified the presence of foramen ovale; in all but one case a right-to-left shunt was noted. In the authors' opinion dangerous regurgitation in these cases is prevented either by (1) the presence of strong trabeculae which might assist in the closure of the tricuspid valve; or by (2) the foramen ovale acting as a safety valve and allowing blood to enter the left auricle (for in one of their cases its surgical closure was followed within a few days by right heart failure); or by (3) "auriculization" of the proximal portion of the right ventricle providing a reservoir for regurgitating blood.

The authors point out that Fallot's tetralogy, pulmonary stenosis, tricuspid atresia, and exudative pericarditis can usually be easily distinguished from Ebstein's disease. Surgical correction of the malformed valve is impossible, and the medical treatment therefore depends, as does the prognosis, entirely on the degree of valvular deformity.

E. S. Wyder

829. **Myocardial Infarction in Infancy: the Surgical Management of a Complication of Congenital Origin of the Left Coronary Artery from the Pulmonary Artery**
D. C. Sabiston Jr., S. Pelargonio, and H. B. Taussig. *Journal of Thoracic and Cardiovascular Surgery* [*J. thorac. cardiovasc. Surg.*] **40**, 321–336, Sept., 1960. 7 figs., 14 refs.

In the majority of cases of myocardial infarction in infancy there is an anomalous origin of the left coronary artery. In this malformation the left coronary artery arises from the pulmonary artery, and infarction has been thought to be due to the supply by the pulmonary artery of blood of low oxygen saturation and under low pressure.

Generally, the condition is diagnosed some weeks after birth and at the latest before the age of 3 months, when symptoms and signs begin to appear. Respiration becomes rapid and difficult, cyanosis may appear, and there may be attacks of vomiting and pallor, suggesting anginal pain. Examination of the chest reveals marked cardiac enlargement; usually no murmur is audible, although a systolic murmur may be heard along the left sternal border. The liver is always enlarged. Chest radiographs show a heart extending on the left side to the

rib margin; pulsation of the left ventricle is markedly diminished. The electrocardiogram is usually characteristic, showing the changes generally associated with myocardial infarction.

Altogether 12 cases of anomalous origin of the left coronary artery from the pulmonary artery with resultant left ventricular myocardial infarction have been seen at Johns Hopkins Hospital, Baltimore. The youngest patient was a neonate and the oldest was 10 months of age. In the first 6 cases in the series operation was not attempted and the infants died before they were one year old. The next 2 cases proved fatal in spite of operation. In a further case it was convincingly demonstrated that the blood in the left coronary artery was flowing into rather than out of the pulmonary artery, and contained arterial blood derived from the right coronary artery through anastomotic channels. This indicated that the damage which resulted from this anomaly was due to valuable arterial blood from the right coronary artery being channelled back into the pulmonary artery through the left coronary instead of supplying the cardiac muscle. At operation, therefore, the left pulmonary artery was tied near its origin from the pulmonary artery in an attempt to obtain a further blood supply to the myocardium, the pericardium was excised, 88% phenol was applied to the pericardium, and the thymus or lung stitched over the heart. Of 3 infants operated on, including one now aged 4, all are developing well.

[It would appear that this operation offers the only chance of survival for the patient with this very serious condition.] *G. S. Crockett*

830. **Neuropathological Findings in Children with Infantile Spasm and Hypsarrhythmia**
E. CHRISTENSEN and J. C. MELCHIOR. *Danish Medical Bulletin* [*Dan. med. Bull.*] 7, 121–127, Oct., 1960. 9 figs., 22 refs.

This paper describes the necropsy findings in 6 cases of infantile spasms with " hypsarrhythmia ", the name given by Gibbs and Gibbs (*Atlas of Electroencephalography*, Cambridge, Mass., 1952) to an electroencephalographic pattern found in certain cases of infantile spasms mainly characterized by forward movements of the head, abduction of the arms, and flexion of the hip-joints and often the knees. The condition has sometimes been called " salaam spasms ". All 6 cases were in boys aged between 8 months and 2 years 5 months. They were divided into two groups with 3 cases in each and with transitional cases between the two groups.

In the first 3 cases there was evidence of exogenous causes such as disease in the mother during pregnancy or difficult delivery. In these 3 cases microcephaly, hydrocephalus, porencephaly, and/or severe gliosis (and in one calcification) were present. In the last 3 cases no evidence of exogenous causes was obtained. However, in one case the mother had influenza during the pregnancy. The brains were of normal size, and hydrocephalus was not present or was very slight. Histological examination revealed developmental abnormalities in both the cortical grey matter of the brain and cerebellum and also in the white matter.

It is suggested that the most probable explanation of the occurrence of hypsarrhythmia in these 6 cases may be that the ganglion cells in the cortical grey matter were abnormal, maldeveloped, or degenerated before maturation. The authors consider that hypsarrhythmia must be regarded as a phenomenon of infancy and not as a disease *sui generis*. It may depend upon the degree of maturation of the nervous system, especially the ganglion cells, and also the age of the patient, so that the syndrome is seen only when there is a discrepancy between age and maturation. *J. MacD. Holmes*

831. **Cataract in Children. Aetiological Aspects in Paediatric Material.** (Katarakt hos barn. Etiologiska synpunkter på ett pediatriskt sjukhusmaterial)
A. BRONGE, B. HAGBERG, and L. MOLIN. *Nordisk Medicin* [*Nord. Med.*] **64**, 1033–1038, Aug. 18, 1960. 27 refs.

The authors discuss the aetiological factors in cataract of various types seen in 25 patients treated at the paediatric clinic of University Hospital, Uppsala, between 1938 and 1959. In 19 cases it was considered to be of prenatal origin, 12 children having had a birth weight of less than 2,500 g. and 15 showing varying degrees of mental retardation, of whom 3 were mongoloid. A history of maternal rubella during pregnancy was obtained in 5 children, and 4 had cerebral palsy probably of prenatal origin. A " placental insufficiency " syndrome was diagnosed in 2 cases and was suspected in several others with dysmaturity. Other congenital anomalies were often present in addition to the cataract. Only one case of zonular cataract, occurring after probable rachitic spasmophilia, and 3 of diabetic cataract were seen.
G. von Bahr

832. **The Nephrotic Syndromes in Childhood.** (Les syndromes néphrotiques de l'enfant)
C. RÉGNIER and H. BOUISSOU. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **17**, 627–646, 1960. 10 figs., 21 refs.

Renal biopsy specimens from 12 children seen at the Paediatric Clinic, Faculty of Medicine, Toulouse, with the nephrotic syndrome were examined by the usual histological methods and also by electron microscopy. The electron-microscopical appearances were of particular diagnostic and prognostic value. In all types of nephrosis the most constant lesion was found in the glomerular epithelium, which showed vacuolization of the cytoplasm and distortion of the " foot-process ". It is pointed out that these changes are not altogether specific, since they have also been seen by the authors in cortical necrosis. In cases of " pure " nephrotic syndrome no alteration in the basal membrane was seen. In these cases the prognosis is quite good, although there is always the danger of further attacks. In " mixed " cases basal-membrane changes leading to marked sclerosis were present and here the outlook was poor.

The authors consider that examination by electron microscopy is a valuable contribution to the diagnosis and prognosis of the nephrotic syndrome.
G. W. Csonka

Medical Genetics

833. **True Idiopathic Hypoparathyroidism as a Sex-linked Recessive Trait**
V. H. PEDEN. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] **12**, 323–337, Sept., 1960. 4 figs., 34 refs.

From St. Louis University School of Medicine and the Cardinal Glennon Memorial Hospital for Children detailed case histories are given of 2 brothers with true idiopathic hypoparathyroidism (T.H.P.). The boys are now aged 2 and 3 years and were first seen with generalized convulsions at 5 days and 7 weeks of age respectively. Both patients satisfy the diagnostic criteria for T.H.P. laid down by Drake and modified by Braisky and are comparable with the 58 cases previously reported from various sources. After examination of the available information the author suggests the classification of the disease into 2 types, one with early onset (10 cases), and the other with late onset (50 cases).

Of the 10 patients with early onset, 8 had convulsions in the first 2 months of life (in the first week in 5 cases), one had tetany in the " newborn period " and convulsions at 9 months, and another convulsions at " a few months less than a year ". All but one of these patients were males and, in addition to the 2 brothers already mentioned, the group includes 3 other brothers. Unfortunately, all that is known about the family of the sibship with 3 affected brothers is that it included an unaffected sister and that the parents were unaffected. A very extensive pedigree has been established by the author for her 2 patients and on the strength of this and the predominance of affected males in all reported cases of early onset she suggests that these represent a distinct type of the disease with sex-linked recessive inheritance. However, it is stressed that T.H.P. of early onset may not be so inherited in all cases and that a much more extensive investigation of pedigrees is required to establish the point.

The pedigree presented in this paper was based on information obtained from the mother and the maternal grandmother of the propositi; it is independently supported by the evidence of a cousin of the maternal grandmother and by the hospital records of the only other persons in the pedigree (2 males) in whom there was definite evidence of T.H.P. The pedigree consists of 4 generations descended from a common pair of ancestors —the great-great-grandparents of the propositi through the female line. It includes in the same generation as the propositi 20 males and 12 females in 13 sibships. In this generation there was, in addition to the propositi, one definitely affected male with an onset of convulsions at 2 weeks. In the preceding generation there were 27 males and 22 females in 14 sibships. This generation included one definitely affected male, who had convulsions at least as early as 9 months of age, 4 males who died of convulsions in infancy, and one male and one female who had convulsions in infancy but did not die. In the generation of the grandparents of the propositi there were 15 males and 11 females in 6 sibships; of these, 7 males died of convulsions in infancy and one male had convulsions in infancy but survived. The sibship which included the great-grandmother of the propositi contained 2 males and 5 females, but no history of convulsions is recorded.

Of the 50 cases in the group with late onset, 8 occurred in only 3 families. It is suggested that these might be classified as cases of " familial late-onset " T.H.P., with sub-groups according to the association with Addison's disease (6 with and 2 without), while the remaining 42 cases might be classified as " non-familial ", with similar subdivision (9 with and 33 without Addison's disease).

The author [rightly] asserts that " more thorough investigation of the ancestry of cases of T.H.P. reported in the future will serve to clarify what is now merely an implied division of T.H.P. into these different types ".

E. A. Cheeseman

834. **Inheritance of Primary Systemic Amyloidosis**
C. E. JACKSON, H. F. FALLS, W. D. BLOCK, J. K. RUKAVINA, and J. H. CAREY. *American Journal of Human Genetics* [*Amer. J. hum. Genet.*] **12**, 434–439, Dec., 1960. 2 figs., 25 refs.

A genetic study of primary systemic amyloidosis is presented as manifested within a large family group. Evidence from this family suggests that the trait is inherited as an autosomal dominant condition. This is in agreement with the impression suggested by the other reported families with this disease.—[Authors' summary.]

835. **A New Autosomal Trisomy Syndrome: Multiple Congenital Anomalies Caused by an Extra Chromosome**
D. W. SMITH, K. PATAU, E. THERMAN, and S. L. INHORN. *Journal of Pediatrics* [*J. Pediat.*] **57**, 338–345, Sept., 1960. 3 figs., 12 refs.

The authors report, from the University of Wisconsin, Madison, the cases of 2 babies possessing an extra autosome in the 16 to 18 group. The infants, one male and one female, died of cardiac failure at 2 and 2½ months of age respectively. The clinical features common to both were probable mental defect, spasticity, micrognathia, malformed and low-set ears, umbilical hernia, intraventricular septal defect, and patent ductus arteriosus. The mothers were both aged 46 at the time of conception.

In an addendum the authors note that they have since seen 4 further children, all unrelated, with the same syndrome, which they now interpret as being trisomy for chromosome 18. They also note that this syndrome appears to be the same as that described by Edwards *et al.* (*Lancet*, 1960, **1**, 787).

C. O. Carter

Public Health and Industrial Medicine

836. ***Pseudomonas pyocyanea* Wound Infection: an Outbreak in an Orthopaedic Unit**
M. Sussman and J. Stevens. *Lancet* [*Lancet*] **2**, 734–736, Oct. 1, 1960. 2 figs., 1 ref.

The authors of this paper from the Departments of Bacteriology and Orthopaedics, Glasgow University, report an outbreak of wound infection due to *Pseudomonas pyocyanea* in 8 patients undergoing treatment for fractures. As a result of extensive bacteriological sampling in the ward and plaster room the source of the infection was traced to the cellulose wadding (wood wool) used as padding under all plaster casts applied to fresh fractures. Moreover, the plaster-encrusted bucket in which plaster-of-Paris bandages were soaked was also contaminated, while an Esmarch bandage used to exsanguinate limbs was heavily infected with various pathogenic organisms, including *Clostridium welchii*. The authors state that " all the wadding has since been autoclaved at 15 lb. [6·8 kg.] (121° C.) for 20 minutes before use and no further incidents of infection have come to light ". *A. Ackroyd*

837. **An Outbreak of Streptococcal Sore Throat due to Infected Milk.** (Massenerkrankung an Angina durch Streptokokken in Lebensmitteln)
H. J. Otte and W. Ritzerfeld. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **85**, 1625–1628, Sept. 9, 1960. 2 figs., 8 refs.

From the Institute of Hygiene, Wilhelms University, Münster, the authors report that 495 out of 1,055 persons employed in two banks in the town suddenly fell ill with tonsillitis. The explosive character of the outbreak resembled that of an epidemic of food poisoning, most of the cases occurring within the space of 2 days. Bacteriological examination revealed the presence of *Streptococcus pyogenes* Group A, Type 9. As far as the authors were able to ascertain, the source of the infection was most probably a rice pudding prepared with uncooked or insufficiently cooked milk, which many of the patients had eaten in the canteen. *Franz Heimann*

838. **Observations on the Epidemiology of Staphylococcal Infections**
K. M. Schreck and E. Hopps. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **240**, 171–185, Aug., 1960. 11 figs., 11 refs.

The pattern of staphylococcal infections encountered at Temple University Medical Center, Philadelphia, was studied over 4 years, 1956–9. The predominant strain of staphylococcus during this period was the Phage Type 80/81, which in the first 3 years caused from 57% to 63% of all infections, the figure declining in 1959 to 38%. A similar decline in the 4th year was found in the infection rate of all categories of infection with this type acquired in hospital. There was in this 4th year an increase in infections caused by other phage types, but no evidence of any new predominant type of staphylococcus replacing Type 80/81.

Antibiotic-sensitivity tests showed changes in sensitivity pattern between 1956 and 1959. Thus there was an increased susceptibility to penicillin by types other than 80/81, to tetracycline by types other than 80/81 and by untypable strains, and to erythromycin by Type 80/81; there was an increased resistance to novobiocin and chloramphenicol by Type 80/81 and by non-typable strains. The nasal carrier rate for Type 80/81 among hospital personnel remained very low, being 4% of 640 persons in 1956 and again 4% of 155 persons in 1959.

Other observations were that no one type of staphylococcus predisposed to bacteriaemia; that hospital-acquired infection rates were the same in diabetics as in non-diabetics; that there was little evidence of a change in the phage type of an infecting organism during the infection; and that, excluding infants, age had probably no influence on the acquisition of an infection. It is concluded that infections more readily occur by person-to-person contact than from the environment.
John M. Talbot

839. **Practical Significance of the Dissemination of Strains of Poliovirus Vaccine Among Contacts of Vaccinated Persons.** (Практическое значение рассеивания вакцинного штамма вируса полиомиелита среди контактировавших с привитыми)
O. V. Barojan and I. N. Gajlonskaja. *Вопросы Вирусологии* [*Vop. Virusol.*] **6**, 532–538, Sept.–Oct., 1960. 3 figs., 6 refs.

The possibility of the spread of virus excreted by subjects given the oral live attenuated poliomyelitis vaccine has been widely discussed and has led to the formation of two schools of thought. The first holds that spread of the attenuated strains is desirable in that it may lead to widespread natural immunization of the population. The second, led by Dick of Belfast (see for example Dick and Dane, *Brit. med. J.*, 1958, **2**, 1184; *Abstr. Wld Med.*, 1959, **25**, 210), sees a potential danger in the natural spread of attenuated poliomyelitis virus, particularly as a slight increase of virulence has been observed in strains which have passed through immunized persons. The recent large-scale use of Sabin's oral live poliomyelitis vaccine in the U.S.S.R. has offered an opportunity to test such theoretical considerations by experimental and epidemiological observations.

For the experimental test two children's homes each with 45 to 55 inmates were chosen. In each, one group of 10 children was immunized with live monovaccine of virus Type 1 after full virological and serological investigations and 4 days later were allowed to mix with the other, non-immunized, children in the home, such contact continuing for 10 days. For the epidemiological observations the town of Kamensk-Uralsk was chosen,

half the population being given oral vaccination with Type 1 and after 2 to 3 weeks vaccine containing virus Types 2 and 3, while the other half received a bland preparation. Altogether 30,235 persons took part in this trial, of whom 15,811 served as controls. A modification of the colour test with monkey kidney tissue was used for the serological tests, while virological investigations were carried out by culturing the strains in monkey tissue cultures and observing the cytopathogenic effect. Isolated strains were typed with poliomyelitis antisera to Types 1, 2, and 3.

Results: In 14 (70%) of the 20 immunized children in the experimental group vaccination was successful, as judged by the serological tests. Of the first contacts of the vaccinees 48% were positive serologically and about 20% of second contacts, while third contacts gave only about 8% positive findings; the serological results in fourth contacts were all negative. Virus was isolated from the faeces in 70% of the vaccinated, but only in 27% of first contacts. No strains were isolated from second, third, and fourth contacts. In the epidemiological study there was one fatal case of paralytic poliomyelitis due to virus of Type 3. This case occurred 15 days after immunization with virus Type 1 and before immunization with Types 2 and 3. No case of poliomyelitis occurred in the large control group. Thus it is concluded that no poliomyelitis occurred in either the immunized or the non-immunized groups that could have been traced back to oral immunization of 14,424 persons with the attenuated live vaccine. *K. Zinnemann*

INDUSTRIAL MEDICINE

840. **The Danger from Dusts Arising during the Sawing of Bricks.** (Le danger des poussières provoquées par le sciage des briques)
G. Proyard. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **21**, 428–431, July–Aug. [received Nov.], 1960.

The use of refractory bricks in industrial processes has greatly increased in recent years. Bricks of aluminium suboxide, silica bricks, and bricks of magnesia all contain quartz, and the shaping of these by means of high-speed mechanical saws produces a dangerous dust. It is true that the number of workers exposed to these dusts is not very great, but in some of them the rapid development of silicosis has been observed, and 2 such cases are cited. In order to prevent this hazard the use of bricks of low silica content is obviously desirable, but this is not always possible. The wearing of a mask and exhaust ventilation are of value, but because of the constantly changing position of the saw there is difficulty in the collection and disposal of the aspirated dust, and even with the use of such ventilation dangerous concentrations of dust have been found to persist. It has been shown that soaking the bricks in an American commercial product known as " Orzan A " (which is a solution of ligneous ammonium sulphate) results in a considerable reduction in the dust concentrations produced by sawing. There appears to be no deleterious effect upon the refractory properties of the bricks thus treated, except that they become somewhat less resistant to crushing.
C. M. Fletcher

841. **Uric Acid Dust as an Aetiological Factor in Occupational Gout.** (Пыль мочевой кислоты, как этиологический фактор профессиональной подагры)
V. S. Luk'janov, I. N. Nikitskij, and N. N. Puškina. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **4**, 6–10, Sept., 1960. 2 figs.

Gout has been described as an occupational disease among workers engaged in the collection, drying, and preparation of dung at poultry farms, an industry which is now carried out on a large scale, the dung being used for the manufacture of uric acid. In spite of the wearing of protective clothing, considerable opportunities exist for the absorption of uric acid through the lungs, gastrointestinal tract, and possibly also the skin.

After doing this work for 2 or 3 years the workers developed pains in the joints, especially of the hands and feet, accompanied by crepitus, while firm, tender tophi in the fingers and toes were observed in some cases. Signs of increased muscular excitation were present and Chvostek's sign was positive. Toothache and dental caries were frequently complained of. The urine contained a high concentration of urates and the blood uric acid level was raised in 43 out of 52 persons examined, the actual values being correlated with the duration of exposure to this type of work. On change of occupation manifestations of the disease disappeared.
Basil Haigh

842. **Maximum Permissible Concentration of Trichlorobenzene in the Air in Working Premises.** (Материалы к обоснованию предельно допустимой концентрации трихлорбензола в воздухе рабочих помещений)
N. M. Vasilenko. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **4**, 16–21, Sept., 1960. 8 refs.

Trichlorobenzene (TCB) is used as a solvent in the aniline dye industry, in the manufacture of condensers and transformers, and also as an insecticide. Symptoms of the toxic action of TCB include headache, nausea, pain in the epigastrium and right hypochondrium, and irritation of the eyes and upper respiratory tract. The signs include vegetative asthenia and neurosis, enlargement and tenderness of the liver, and in the blood neutropenia with a relative lymphocytosis.

Clinical and environmental investigations suggested that the health of workers is adversely affected by prolonged exposure to concentrations of TCB of 0·1 to 1·0 mg. per litre of air. In laboratory investigations the effect of concentrations of TCB of the order of 0·1 mg. per litre was studied in rats, which were exposed to the agent for various periods after which the reflex activity and state of the blood were investigated. These experiments revealed abnormalities in the animals, notably pronounced changes in the functional state of the central nervous system, from which it is concluded that the maximum permissible concentration of TCB in the atmosphere of working premises should be below 0·1 mg. per litre of air. *Basil Haigh*

Forensic Medicine

843. **The Subjective Syndrome in Cranial Trauma.** (Le syndrome subjectif des traumatisés crâniens)
L. COTTE. *Annales de médecine légale et de criminologie, police scientifique et toxicologie* [*Ann. Méd. lég.*] **40**, 422–432, Sept.–Oct. [received Dec.], 1960.

No settled consensus of opinion has yet been reached on the pathological basis of the subjective symptoms that in many cases follow cranial trauma. It has been shown that these symptoms are not directly related to the amount of tissue damage, and indeed they are somewhat less frequent in cases of head injury in which the skull has been fractured than in those without such fracture.

Writing from the Department of Forensic Medicine and Deontology, Lyons, the author recalls that the symptoms show great variation in character, severity, and persistence. The commonest features are headaches, vertigo, visual and auditory disturbances, and difficulty in mental concentration. The headaches tend to be chronic, are readily exacerbated by noise or fatigue, are often accompanied by a feeling of weight or constriction, are usually susceptible to relief by analgesics, and lack the pulsating quality associated with headaches of vascular origin. The patient has to make an effort to focus his eyes for any length of time, and thus visits to the cinema and looking at television are poorly tolerated. In addition the hearing tends to be painfully hypersensitive. The patient may also complain of memory loss, and in particular of difficulty in recall when occasion demands. The most common emotional changes are excessive irritability and outbursts of bad temper.

The symptoms are not necessarily accompanied by any demonstrable physical changes, although neurological signs and electroencephalographic abnormalities should be looked for. In the differential diagnosis the uncomplicated subjective syndrome has to be distinguished from post-traumatic neurosis, in which the symptoms appropriate to cerebral trauma are overlaid by diverse neurotic complaints. The variability in the severity and duration of the syndrome, the frequent absence of physical signs, and the bearing which the disability may have on the type of work the patient does combine to present a complex problem when questions of legal compensation are under consideration.

[In some ways this is a disappointing paper.]

D. J. West

844. **A Statistical Study of Suicide in the City of Milan.** (Commento a rilevazioni statistiche sul suicidio nella città di Milano)
P. POZZATO. *Ospedale maggiore* [*Osped. maggiore*] **48**, 352–365, Aug. [received Oct.], 1960. 2 figs., 5 refs.

In this paper the author presents a statistical analysis of the suicides and attempted suicides occurring in the city of Milan during two different periods, namely, the decennium 1924–33 (Period A) and the quinquennium 1955–9 (Period B). He selected these periods as representing two during which the tenor of life was more or less even and so less likely to influence adversely the suicide rate.

In Period A attempts at suicide were made by 2,029 males and 1,795 females, while in Period B the figures were 861 males and 1,333 females, the marked inversion in numbers being noteworthy. For actual suicides, in Period A the numbers were 1,333 males and 470 females and in Period B 406 males and 232 females. In Period A the most common ages for attempted suicide were 20 to 30, followed by 30 to 40, and then 10 to 20, whereas in Period B the order was 20 to 30, 30 to 40, 40 to 50, and lastly 10 to 20. For actual suicides no ages are given for Period A; in Period B the highest number occurred in age group 55–64, followed closely by age group 45–54. In regard to methods employed, in the unsuccessful suicides in Period A the ingestion of solids and liquids was 5 times as frequent as any other method, firearms came next, then hypnotics and analgesics, poisoning by coal-gas being 6th on the list. In Period B on the other hand, hypnotics and analgesics were used twice as frequently as any other means, followed by ingestion of solids and liquids, then coal-gas, with cutting and stabbing equal in 4th place, firearms being relegated almost to the bottom of the table. For the actual suicides during Period A firearms were used most often, next poisoning, followed by jumping from a height. (No comparative details are given for Period B.) It is noted that most attempts at suicide in Period A were made by domestic servants, and these together with other [? general] workers made up more than 50% of the persons involved. [The total number of attempts in the author's Table 4 differs from the numbers given elsewhere in the text.] In Period B domestic servants again made most attempts, followed by clerical workers, female dressmakers, and clothing workers in that order. The proportion of suicidal attempts, in relation to the total, made by students rose sharply in Period B, and in this period also more females made attempts than males. The author also presents evidence to demonstrate some possible meterological or seasonal factor, the number of attempts being greater in the summer months, though they fell off sharply in August, which is the holiday month in Milan. The increase in attempts by females (and the relative increase in actual suicides by women) can partly be ascribed to the considerable increase in the part women now play in everyday affairs, especially in business, the strain of which, it is suggested, may lead to depressive crises.

[There has been so much change in social conditions in the last 30 years that the two periods are scarcely comparable, and so far as suicide is concerned the much greater availability of hypnotics and coal-gas vitiates such a comparison. Further the omission of the ages of those committing suicide in Period A and of the methods employed in Period B greatly detract from the value of the paper.] *W. K. Dunscombe*

Anaesthetics

845. **Premedication with Atropine by Mouth**
M. C. JOSEPH and R. J. VALE. *Lancet* [*Lancet*] **2**, 1060–1061, Nov. 12, 1960. 6 refs.

A trial of the oral administration of atropine preoperatively in children is reported from Guy's Hospital, London. A total of 147 children admitted under the same surgeon and anaesthetist for tonsillectomy were given atropine by random selection either by mouth or by subcutaneous injection. The average interval between administration of atropine and induction of anaesthesia was 95 minutes when the drug was given by mouth and 87 minutes when given subcutaneously. The dosage was 0·05 mg. of atropine by mouth or 0·64 mg. subcutaneously —with 75 mg. of butobarbitone per 14 lb. (6·3 kg.) body weight. All the patients were anaesthetized with ether after induction with ethyl chloride on a Schimmelbusch mask or nitrous oxide and oxygen through a semi-open circuit. The sleeping pulse rate on the night before operation was recorded and the pulse rate was taken again just before the patient was taken to the theatre. The size of the pupils was measured in the anaesthetic room. The degree of salivation was estimated by inserting a finger into the buccal sulcus during induction.

The mean pulse rate before atropine and the rise in the pulse rate after atropine were similar in both groups. The average size of the pupils was identical in the two groups, and excessive salivation was uncommon in both. It is concluded that atropine by mouth is as effective as atropine by subcutaneous injection. *M. Woods*

846. **Alterations in Response to Somatic Pain Associated with Anaesthesia. I: An Evaluation of a Method of Analgesimetry**
J. W. DUNDEE and J. MOORE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 396–406, Sept., 1960. 8 figs., 16 refs.

After referring to various methods previously used for the experimental production and measurement of pain the authors describe in detail the method they have adopted at Queen's University, Belfast. This is based on the principle described by Clutton-Brock (*Brit. J. Anaesth.*, 1957, **29**, 111) of applying gradually increasing pressure to the front of the tibia by means of a round-headed screw which replaces the tray of a household spring balance, and recording the scale reading when pain is first felt. The present authors, however, use a brass disk 9·2 mm. in diameter in place of the screw, and the number of applications is limited to 4 or 5 in order to avoid soreness. Moreover, readings are made at two clearly defined end-points—a " threshold " reading when the pain is first felt and a " response " reading when it becomes intolerable or there is withdrawal of the leg. The readings are recorded in " pain units ", one unit corresponding to a pressure of 1 lb. (0·45 kg.) as indicated on the scale of the spring balance used.

In the investigations reported in this series of papers certain variables were recognized and countered. The rate of application was standardized so that a pressure of 7 lb. (3·175 kg.) was reached in about 10 seconds and 14 lb. (6·35 kg.) in about 30 seconds. One limb only was used, since preliminary observations showed an occasional difference between readings made on the two legs of the same subject; duplicate readings were taken when possible. Control readings taken at hourly intervals proved consistent up to 3 hours, but similar observations made at longer intervals (up to 33 days) showed considerable variation. The effects of suggestion, distraction, and impatience on the subject were carefully avoided, and prejudice on the part of the observer was eliminated by a " blind " technique in the comparison of different analgesics. Since the postoperative reading on patients with a painful wound was invariably found to be lower than the preoperative reading, only patients undergoing such procedures as endoscopy or dilatation and curettage were used for the study of postoperative response to pain. It was found that hypotension induced by the administration of certain drugs also affected the results and all cases in which hypotension occurred were therefore excluded. In preliminary readings on 100 male and 200 female subjects statistically significant evidence was obtained of a higher pain threshold in men than in women under normal conditions. A very wide scatter of both threshold and response readings was also found, indicating that " each person must serve as his own control in assessing the effect of drugs ".

The effects of pethidine given intravenously in doses of 100 mg. were studied in 9 subjects, the drug being given slowly (over 5 minutes) to avoid inducing hypotension. Analgesia could not be demonstrated until about 10 minutes after the injection and the threshold readings were affected more than the response readings. When the same dose was given intramuscularly to 71 subjects analgesia appeared after about 45 minutes, reached its peak after 75 to 90 minutes, and lasted not more than 6 hours. It was also observed that the highest analgesic responses were elicited in those subjects, both male and female, with the lowest initial threshold readings. It therefore appears that the initial threshold to pain must be taken into account in evaluating the analgesic potency of a drug by this method. On the other hand, provided subjects with a high initial threshold reading are considered separately from those with a low reading, " sex can be ignored as a factor likely to influence the response to analgesics ". *Michael Kerr*

847. **Alterations in Response to Somatic Pain Associated with Anaesthesia. II: The Effect of Thiopentone and Pentobarbitone**
J. W. DUNDEE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 407–414, Sept., 1960. 8 figs., 9 refs.

Using the method previously described [see Abstract 846], the author has studied the anti-analgesic effects of thiopentone in 73 patients, most of whom were

undergoing dilatation and curettage. Pethidine was given preoperatively to 38 of the patients and in some cases the anaesthesia induced by thiopentone was maintained with nitrous oxide and oxygen. Observations were made immediately before the administration of thiopentone and again 30 seconds (and in some cases 60 seconds) afterwards. In an unstated number of subjects observations were also made during the postoperative period. In 10 cases similar studies were made of the anti-analgesic effect of pentobarbitone. The author summarizes his findings as follows.

"Small doses of thiopentone and pentobarbitone in the order of 0·6 to 1·5 mg. per kg. will result in increased sensitivity to somatic pain. The action of thiopentone can be detected half-a-minute after injection and lasts for only a few minutes. With pentobarbitone there is a delay of at least 1 minute after intravenous injection before the maximum anti-analgesic action can be demonstrated. It is suggested that these differences are due to different rates of penetration of the two drugs into the brain. With larger doses of thiopentone the pain threshold will rise but only after the patient becomes unconscious. A marked anti-analgesic action has been demonstrated in the recovery period up to 5 hours after injection of commonly used doses of thiopentone. The duration of this action is even more prolonged after similar doses of pentobarbitone are given. Small doses of thiopentone antagonize the analgesia produced by 100 mg. of pethidine and on occasions it was possible to demonstrate an antagonism to nitrous oxide analgesia. Results suggest that the analgesia produced by 50% nitrous oxide with oxygen mixtures is more pronounced than that which follows the intramuscular or intravenous injection of 100 mg. of pethidine. The data presented offer a possible explanation for the postoperative restlessness which follows the premedicant use of barbiturates in children, especially when a painful wound is present. It is suggested that, on theoretical grounds, this is an unsatisfactory form of pre-anaesthetic medication." *Michael Kerr*

848. **A Combination of Analgesic and Antagonist in Postoperative Pain**

G. Hossli and G. Bergmann. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 481–485, Oct., 1960. 2 refs.

The authors describe a series of studies designed to establish whether the addition of a small quantity of the narcotic antagonist levallorphan reduces the respiratory depressant action of pethidine. They also investigated the effect on analgesic activity and on the incidence of side effects.

The study of respiratory depression was carried out in two groups of anaesthetized patients. When anaesthesia was established each patient was given a dose of pethidine 1 mg. per kg. [body weight] alone or mixed with levallorphan in the proportion of 80:1. The results showed that there was a statistically significantly smaller reduction of the respiratory rate, minute volume and alveolar ventilation in the pethidine plus levallorphan group.

To investigate the analgesic activity two groups of patients with postoperative pain were treated in a blind control study with either pethidine or pethidine with levallorphan in the above proportion. It was found that the average analgesic activity was almost the same with the two types of treatment. The incidence of side effects between the two groups was insignificantly different.

The authors conclude that the addition of levallorphan in the above proportion gives almost complete protection against the respiratory depressant effect of pethidine without diminishing the analgesic effect and without increasing the incidence of side effects.—[Authors' summary.]

849. **A Preliminary Report on Postoperative Use of Vesprin by Drip Method**

B. Sheiner. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 435–437, Sept.–Oct., 1960. 5 refs.

The postoperative use of "vesprin" (trifluoproma zine) was investigated at Pasack Valley Hospital, Westwood, New Jersey, on 100 patients, aged 15 to 72 years, most of whom had undergone abdominal surgery. Anaesthesia had been induced with thiopentone and maintained with ether or cyclopropane or a combination of the two. Each patient received 20 mg. of trifluopromazine diluted to 1,000 ml. with 5% glucose solution as a continuous infusion at a rate of 40 to 60 drops per minute during the immediate postoperative period. A comparable series of 100 patients given 1,000 ml. of 5% glucose infusion postoperatively served as controls.

The patients given trifluopromazine remained lightly asleep for some time after the operation, but could be roused. Only 26 required analgesics for pain in the first 6 hours, as against 95 of the control patients. As many as 76 of those who received trifluopromazine had little or no memory of events in the 12 postoperative hours, compared with only 9 in the control group. On the other hand 62 of them developed postoperative hypotension, as against 30 of the controls. The incidence of nausea and vomiting was much reduced in the medicated patients. *Mark Swerdlow*

850. **Changes in Pulse Rate and Rhythm Associated with the Use of Succinylcholine in Anesthetized Children**

N. W. B. Craythorne, H. Turndorf, and R. D. Dripps. *Anesthesiology* [*Anesthesiology*] **21**, 465–470, Sept.–Oct., 1960. 2 figs., 6 refs.

In infants and children bradycardia and cardiac arrhythmias may occur after intravenous administration of succinylcholine, but not after intramuscular injection of the drug. In this paper from the University of Pennsylvania School of Medicine, Philadelphia, the response of 29 children to intravenous administration of a single dose of succinylcholine is described. Bradycardia occurred in 17 and cardiac arrhythmias in 6. In 6 additional patients who received repeated doses the bradycardia was more marked. Belladonna drugs given preoperatively appeared to reduce these cardiac effects. The authors suggest that deep anaesthesia may give some protection against this action of succinylcholine. No change in cardiac rate or rhythm was noted when the drug was given intramuscularly. *W. Stanley Sykes*

Radiology

851. **Circulatory Disturbances during Cerebral Angiography: an Experimental Evaluation of Certain Contrast Media.** [In English]
E. KAGSTRÖM, P. LINDGREN, and G. TÖRNELL. *Acta radiologica* [*Acta radiol.* (*Stockh.*)] **54**, 3–16, July, 1960. 5 figs., 25 refs.

The authors set out to determine the effect upon the rate of cerebral blood flow of injection of various types of contrast media normally used in cerebral angiography.

In 7 anaesthetized dogs the blood flow in the cerebral circulation was measured by interposing a drop chamber and photo-electric recording unit into the path of the common carotid artery; just beyond this side-loop contrast medium was injected through a fine polythene catheter. To restrict the field of investigation to the cerebral vessels only, the external carotid artery was ligated and, in order to preserve normal physiological function in the region supplied by this vessel, an anastomosis to the brachial artery was made beyond the ligature. As a second method of estimation the rate of venous outflow from the sagittal sinus was concurrently measured in some cases. The response in terms of cerebral flow, as shown by the sagittal venous return, in all cases ran parallel to that measured by the drop chamber, but tended to be less pronounced. This difference is explained by the fact that the venous return drained a larger area than that immediately supplied by the medium injected.

The contrast media tried were diodone, " hypaque " (sodium diatrizoate), " miokon " (sodium diprotrizoate), and sodium acetrizoate. It was found that the increase in cerebral blood flow was greatest when sodium acetrizoate or diodone was used, the increases being respectively 370% and 235% of the resting level. Much less effect was obtained with sodium diatrizoate or sodium diprotrizoate, the increases never exceeding 100% of the resting level.

Finally, as a check on the actual distribution of the medium injected some angiograms were taken with a larger volume of medium and higher pressure. These showed that the distribution of the medium was mainly intracerebral; any extracerebral vessels filled, therefore, would not be likely to play any important part. [This probably did not even occur in the circumstances of the actual experiment, where a smaller volume of medium was used.] *A. M. Rackow*

852. **Value of Different Projections in Diagnosing Cholesteatoma.** [In English]
G. JENSEN, C. JESPERSEN, and S. BRUNNER. *Acta radiologica* [*Acta radiol.* (*Stockh.*)] **54**, 177–185, Sept., 1960. 5 figs., 18 refs.

Reports in the literature show that radiologists are not agreed about the value of the various projections which are used for demonstrating destruction of the temporal bone in chronic infection of the middle ear. Many projections which have been developed from Schüller's and Stenvers's views have the disadvantage that the attic and antrum are superimposed on the dense bone around the semicircular canals and cochlea. The Chaussé III projection avoids this disadvantage and also demonstrates the lateral wall of the attic and superior wall of the external auditory meatus.

Writing from the Sundby Hospital, Copenhagen, the authors describe their experience with the Schüller, Runstrom III, and Chaussé III projections in 80 cases of chronic otitis media in which bone destruction had been found at operation. The main results are summarized in the following table, in which the numbers of positive findings with Schüller's projection are given in Column A, those with the Runstrom III projection in Column B, and those with the Chaussé III projection in Column C. All the patients were examined with all three projections.

Operative findings	No.	Projection		
		A	B	C
Site of cholesteatoma:				
Antrum	41	14	11	22
Antrum + attic	36	18	10	26
Attic	3	—	—	2
Total ..	80	32	21	50
Complications:				
Fistula of labyrinth ..	6	—	—	1
Denuded dura	4	—	—	—
Size of bone destruction:				
Hazel nut and greater ..	50	26	17	39
Pea	3	1	2	3
Dilated antrum and attic..	27	5	2	8

This shows that while a cavity must have reached a certain size before it can be demonstrated radiographically by any of the three projections, the Chaussé III contributes more information than the other two. In the authors' experience, if antero-posterior tomography is also used bone destruction can be diagnosed in up to 80·9% of cases. *Michael C. Winter*

853. **Xeroradiography of the Breast**
H. R. GOULD, F. F. RUZICKA JR., R. SANCHEZ-UBEDA, and J. PEREZ. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 220–223, Aug., 1960. 4 figs., 10 refs.

Soft-tissue radiography of the breast as a diagnostic measure has been used with some success, but this has been limited by difficulties of technique. In this report from St. Vincent's Hospital of the City of New York the authors describe the use of xeroradiography as a method of investigation in this field, based on a study of

13 female patients selected at random. Instead of film a selenium-coated and charged metal plate is used. With a wider latitude of radiological factors satisfactory images can be obtained by dusting the plate with charged calcium carbonate powder. It is considered that this method has advantages over conventional radiography because the resolving power of the xeroradiographic plate is greater and also the range of contrast is much less. The resulting images can be preserved by an adhesive technique; they may also be photographed, with slight consequent loss of detail. *R. O. Murray*

854. **Intercostal Lung Bulging, an Early Roentgen Sign of Emphysema in Children**
S. SCHORR and D. AYALON. *Radiology* [*Radiology*] **75**, 544–551, Oct., 1960. 6 figs., 16 refs.

Normally the line separating the edge of the lung from the soft tissues on a postero-anterior chest film is straight or slightly concave, but in children with acute emphysema the lung bulges outwards slightly between the ribs. The authors investigated this sign at the Municipal Hospital " Hadassah ", Tel-Aviv, Israel, by comparing the radiographs of 27 children under the age of 3 who had respiratory infection with those of 50 controls (aged under 20 months) who had no respiratory disturbance. Four of the control series showed the sign, but 3 of them were found to have had a respiratory infection. The appearance was reversible in some cases, while in 5 patients who died the emphysema was confirmed at necropsy. The lateral radiographs in some cases also showed paraspinal bulging, which was occasionally present without the other sign. *D. E. Fletcher*

855. **One Hundred Consecutive Cases of Dysphagia: Some Problems in Diagnosis**
G. OSBORNE, P. T. SAVAGE, and S. L. STRANGE. *Clinical Radiology* [*Clin. Radiol.*] **11**, 250–265, Oct., 1960. 22 figs., 9 refs.

A consecutive series of 100 cases of dysphagia examined radiologically by one of the authors at the Whittington Hospital, London, over a period of about 4 years is surveyed. [No comparative figure, such as the total number of barium-meal examinations performed or the number of cases of gastric carcinoma diagnosed by the author during the same period, is given.] All but one of the 100 patients were originally referred with dysphagia of unknown cause—that is, patients with dysphagia due to such causes as scleroderma and the terminal stages of bronchial carcinoma were excluded, as were also those referred to the Ear, Nose, and Throat Department with a " lump in the throat " which persisted independently of swallowing.

In 34 cases malignant disease was diagnosed; in 19 the primary growth was in the stomach; in 11 there was a squamous carcinoma of the oesophagus which in 5 cases was near the cardia; and in no less than 4 cases the obstruction was secondary to a silent primary in the bronchus. In 4 of the cases of gastric carcinoma and 3 of those of oesophageal carcinoma there was an associated sliding hiatal hernia. [The question which came first is not discussed.] The difficulty of distinguishing between malignant strictures and those due to peptic oesophagitis is emphasized. Smooth strictures may be malignant (2 out of 11 in this series), while irregular ones may be benign and even repeated biopsies by experienced surgeons are fallible: the working rule suggested is to assume that irregularity associated with a stricture denotes malignancy even if biopsy is negative.

Reflux oesophagitis was diagnosed in 29 cases, with a definite stricture in 14. In 8 cases a sliding hiatal hernia was the presumptive cause, and in 5 the stricture followed total or partial gastrectomy (a hernia also being present in one of these). In one case, that of a man of 82, no explanation is offered. In 15 cases there was no stricture, but oesophagitis was probable—in 14 of these the presence of a sliding hiatal hernia was proved and in the 15th case the examination was unsatisfactory, the patient being an elderly woman with a fracture of the neck of the femur who subsequently recovered.

In 21 cases no cause for the dysphagia could be found; 13 of these patients, aged 39 to 80, had a short history, and the possibility of a lesion was excluded by necropsy, recovery, or the length of follow-up. The remaining 16 cases consisted of 6 examples of achalasia, 4 of small paraoesophageal herniae, 2 of pharyngeal pouch, one of Paterson–Kelly webb, one of dysphagia secondary to a healed benign gastric ulcer, one in which dysphagia started after a cerebrovascular accident and rapidly improved, and one in which dysphagia was ascribed to compression of the oesophagus between a dilated heart and a tortuous aorta.

[Fashion leads to papers of this type being unjustly neglected. They are very valuable. The junior radiologist knows more about possibilities than probabilities and the senior radiologist is only too likely to miss a diagnosis if he believes it to be much rarer than it is. There is no mention in this paper of the frequency with which a distended splenic flexure of the colon displaces the stomach to the right and leads to voluntary or involuntary belching, reflux, and possibly transient oesophagitis and a sliding hernia.] *Denys Jennings*

856. **Roentgen Manifestations in Progressive Systemic Sclerosis (Diffuse Scleroderma)**
B. GONDOS. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 235–247, Aug., 1960. 8 figs., 34 refs.

Diffuse scleroderma is a progressive disease of connective tissue which leads to prolonged disability and is often fatal. Any organ may be affected, the sequence of events being always the same—oedema, followed first by connective-tissue proliferation and sclerosis of collagenous bundles, and finally by atrophy. In this report from the General Hospital, Washington, D.C., the author reviews 25 cases seen over the last 16 years and considers the radiological changes encountered in the light of accounts in the literature.

The heart is often enlarged and triangular, with diminished pulsation, and at necropsy the cardiac muscle shows irregular areas of fibrosis not related to disease of the coronary arteries; the heart was affected in 8 of the present cases. In the lungs, affected in 7 cases,

there is diffuse interstitial infiltration with degenerative cystic lesions; these may expand into pneumatoceles and their rupture may cause a pneumothorax. The author considers this pulmonary fibrosis to be a primary manifestation of the disease. The alimentary tract was involved in 14 cases, this being characterized by dilatation and decreased intestinal peristalsis, with delay in transit of barium. Such changes are most common in the oesophagus; they were also observed in the small intestine and colon, but no striking abnormalities were seen in the stomach. Bone abnormalities, present in 6 cases, frequently resulted in absorption of the terminal phalanges of the fingers and, less commonly, those of the feet. Similar changes were noted in the distal ends of the radius and ulna. Attempted remodelling during quiescent phases may produce a conical deformity of the affected bone ends. The presentation of the disease by joint symptoms may be attributed to involvement of synovial membranes. Skin contractures often result in subluxations and dislocations of the interphalangeal and metacarpo-phalangeal joints. Calcinosis of the soft tissues was also observed 4 times in the present series. Marked thickening of the periodontal membrane, when this occurs, provides a strong radiological indication of the disease. *R. O. Murray*

857. **Roentgenologic Findings in Familial Mediterranean Fever**

N. SHAHIN, E. SOHAR, and F. DALITH. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 269–274, Aug., 1960. 6 figs., 10 refs.

Familial Mediterranean fever is limited to certain ethnic groups, mainly Jews and Armenians, and appears to be based on a recessive hereditory gene. Since, radiologically, the disease may resemble tuberculous pleuritis, intestinal obstruction, or tuberculous or rheumatoid arthritis, the authors describe the x-ray appearances in 40 cases seen at the Tel-Hashomer Hospital, Tel-Aviv, Israel.

They state that the disease may be manifested in one of three ways: by abdominal attacks, by chest attacks, or by acute affections of one or more of the larger joints. In the abdomen the attack clinically may take the form of a peritonitis, and radiologically may show some degree of ileus in the small or large bowel, with gas and fluid levels. In the chest it is common to find a pleural reaction with effusion; this effusion is not usually large and tends to resolve in a few days. The joint involvement, which may be accompanied by synovial effusion, may in the early stage show no radiological change, but when the attack is more protracted subperiosteal osteoporosis may develop, and in the later stages degenerative changes in the cartilage followed by erosion of the bone may be found. The main point of differentiation from rheumatoid arthritis is that the small joints are not usually involved, the sacro-iliac, hip-, and knee-joints being mainly affected.

Characteristically the disease proceeds by attacks and remissions, and no effective treatment is at present known. *A. M. Rackow*

858. **Impression of the Left Atrium on the Superior Vena Cava and Sinus of the Venae Cavae in Mitral Disease.** [In English]

G. F. GARUSI. *Acta radiologica* [*Acta radiol. (Stockh.)*] **54**, 265–272, Oct., 1960. 5 figs., 11 refs.

The author describes the topographical relations of the left atrium in cases of mitral disease, with special reference to the superior vena cava and the sinus of the venae cavae, as demonstrated by angiocardiography at the Roentgen Institute of the University of Bologna. The subjects studied were 9 patients with mitral disease, which in some was associated with other cardiac lesions.

The left atrium is held down on both sides by the pulmonary veins and can consequently expand only transversely or in the sagittal plane. In the asthenic or flat type of chest enlargement will occur mostly in the transverse direction. The orientation of the heart in the thorax and the size of the other chambers also influence the direction of atrial expansion. On angiocardiography an increase in the transverse diameter is seen in the frontal projection as a displacement of the lateral margin of the left atrium to the right, with the formation of a double outline on the right side of the heart. Widening of the bifurcation of the trachea with upward displacement of the main bronchi, particularly the left, is also seen, and a regular impression will be seen along the left border of the lower third of the barium-filled oesophagus. An increase in the sagittal diameter is seen in the lateral projection as a posterior displacement of the oesophagus; anteriorly, the left atrium presses on the lower part of the superior vena cava and the posterior wall of the upper half of the right atrium, corresponding to the so-called " sinus " of the venae cavae. The size of the impression caused by the left atrium depends on the degree of its enlargement and on the sagittal diameter of the thorax.

Reflux into the arch of the azygos vein occurred in 6 of the author's 9 cases. This sign might be interpreted as being due to a decreased blood supply in the superior vena cava or, in part, to compression of the enlarged left atrium, but is mostly due to the high right endoatrial pressure in mitral disease, which is further increased by the injection of contrast medium. Reflux also occurred into the inferior vena cava, but this was not proportional to the size of the impression of the left atrium or to the amount of reflux into the azygos vein. Its occurrence might depend on whether or not the axis of the two venae cavae is perpendicular.

John H. L. Conway-Hughes

859. **Spinal Cord Injury as a Complication of Aortography**

D. A. KILLEN and J. H. FOSTER. *Annals of Surgery* [*Ann. Surg.*] **152**, 211–230, Aug., 1960. 2 figs., bibliography.

A number of cases of damage to the spinal cord following aortography have been reported in the literature. From this source and from a card inquiry sent to doctors attending patients suffering such injury the authors of this paper from Vanderbilt University School of Medicine, Nashville, Tennessee, collected a total of 38 cases and, in response to a questionary, considerable detailed informa-

tion concerning 28 of them. The damage appeared to affect motor fibres rather more than the sensory and in nearly all the cases paraplegia was the dominant symptom; sensory changes were present in varying degree and there was complete paralysis in 19 cases. Evidence of return of motor function was observed in 13 of the 28 patients and 5 of these ultimately recovered completely with no residual weakness. Post-mortem examination was possible in 6 patients who died at intervals varying from 2 days to 17½ months after the injury. In 3 of these there was some softening of the spinal cord, but no evidence of injury or thrombosis was detectable in the aortic wall or the segmental or spinal arteries.

The contrast medium used varied; in 21 cases "urokon" (sodium acetrizoate) was the medium, while in the others "diodrast" (diodone), "neo-iopax" (sodium iodomethamate), or "hypaque" (sodium diatrizoate) was used. The amount injected varied from 10 to 45 ml.; when injections were repeated the highest total quantity of contrast medium given was 84 ml.

The authors discuss the mechanism of the damage to the cord and conclude that this is a toxic effect of the contrast medium acting directly upon the cells of the grey matter. They recommend certain measures to safeguard against the occurrence of brain injury: (1) the use of the least toxic contrast medium, which, in their view, is hypaque 50%; (2) a single injection of the medium; (3) examination of the patient in the prone rather than in the supine position; (4) the use of the smallest volume of contrast medium which will give an adequate radiological picture; and (5) avoidance of barbiturate anaesthesia.

A. M. Rackow

860. **Significance of Repeat Injection of Contrast Medium in the Genesis of Kidney and Spinal Cord Damage Resulting from Abdominal Aortography**

D. A. KILLEN and E. M. LANCE. *Annals of Surgery* [*Ann. Surg.*] **152**, 231–239, Aug., 1960. 7 figs., 11 refs.

One of the factors which is believed to increase the risk of damage to the kidneys and spinal cord following aortography is the repetition of an injection of the contrast medium a short time after the initial injection. In a series of experiments on dogs "diodrast 70%" (diodone), "miokon 90%" (sodium diprotrizoate), or "hypaque 90%" (sodium diatrizoate) was injected into the abdominal aorta at laparotomy, the animals being supine and anaesthetized with veterinary "nembutal" (pentobarbitone). The object of the experiment was to determine the toxic effects of the media on renal function and on the spinal cord in animals given a single injection and in others given a repeat injection within 15 minutes of the first.

Of the 55 animals included in the experiments, 41 survived beyond the 6-day period necessary for determining renal function, which was based on the non-protein nitrogen level in the blood, values over 45 mg. per 100 ml. indicating impaired renal function. In 2 out of 24 animals given a single injection and in 6 out of 22 given a second injection there was impaired renal function. Of the latter group of 6, none had received hypaque; the toxic effects on the kidneys followed injection of diodone in 5 and of miokon in one.

The toxic effect on the spinal cord was demonstrated by the occurrence of immediate reactions, varying from hyperextension of the hind legs and clonic seizures to a state of increased reflex excitability, after which varying degrees of motor paralysis developed. Analysis again showed that the incidence of spinal-cord damage was higher in animals receiving a second injection.

Of the three agents used diodone proved to be the most toxic to renal tissue, while miokon appeared to be the most toxic to the spinal cord; hypaque was the least toxic to both these structures. The authors consider that the effects demonstrated could be due to an increased permeability of the vascular bed caused by the first injection, this rendering the toxic potential of the second greater.

A. M. Rackow

861. **A Renal Cortical Index Obtained from Urography Films**

P. VUORINEN, L. PYYKÖNEN, and P. ANTTILA. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 622–626, Oct., 1960. 3 figs., 8 refs.

The authors of this paper from the Central University Hospital, Turku, Finland, describe a method of calculating a "renal cortical index" (R.C.I.) from intravenous pyelograms. The R.C.I. is obtained by dividing the product of the length and breadth of the pelvis-calyces system by the product of the length and breadth of the kidney itself, the measurements being taken on antero-posterior intravenous pyelograms. It is thus a method of expressing the ratio between the area of the pelvis and calyces and the renal parenchyma. The technique has been used in 118 patients, 58 of whom were considered clinically to be normal and 60 abnormal. In the normal patients the mean R.C.I. was 0·37, while in the abnormal patients it was 0·44.

The patients were divided into three groups: (1) those for whom data for the serum creatinine level were available; (2) those for whom reliable results from direct renal function tests were not available, but who were classified as normal or abnormal on the basis of clinical findings; and (3) patients who had unilateral renal calculi and in whom the R.C.I. on the two sides was compared. In all these cases the R.C.I. was significantly higher in the abnormal than in the normal kidneys.

The authors consider that these preliminary results indicate that the R.C.I. tends to rise in pathological conditions, that it is an indication of the functional capacity of the kidney, and that the upper limit of normal is in the region of 0·4.

Arnold Appleby

862. **Double-contrast Cystography in Tumours of the Urinary Bladder.** [In English]

O. BARTLEY and C. G. HELANDER. *Acta radiologica* [*Acta radiol.* (*Stockh.*)] **54**, 161–169, Sept., 1960. 10 figs., 7 refs.

Neoplasms of the urinary bladder tend to have a more irregular surface than that of the normal distended bladder wall and therefore double-contrast cystography, in which two media of different radio-density are used to demonstrate the mucosal pattern, is more likely to demonstrate the presence of a vesical neoplasm than

cystography with a single contrast medium. The authors of this paper from Sahlgrenska Sjukhuset, Gothenburg, Sweden, use 200 to 300 ml. of carbon dioxide and 8 to 10 ml. of a liquid opaque medium; they have found "dionosil aqueous" (a 50% suspension of propyliodone) the most satisfactory liquid medium. After the media have been introduced into the bladder the patient is rotated so that the dionosil will adhere to the mucosa. Carbon dioxide is 30 times more soluble in plasma than is oxygen and there is therefore little danger of gas embolism.

In a series of 75 double-contrast cystographies there were no complications. Twenty of the examinations were performed on patients with verified bladder tumour, and in all these cases the tumour was demonstrated; papillomata were most easily seen, but tumours as small as a rice grain were demonstrated. Not only may the situation of a tumour be determined by this method, but also its nature may be inferred, as those features which favour a diagnosis of malignancy—a sessile non-papillomatous appearance and an ill-defined edge—are more readily demonstrated than by the ordinary technique.

Michael C. Winter

863. **Diagnostic Accuracy of the Barium Enema Study in Carcinoma of the Colon and Rectum**
R. N. COOLEY, C. H. AGNEW, and G. RIOS. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **84**, 316–331, Aug., 1960. 7 figs., 18 refs.

The authors, at the University of Texas, Galveston, have reviewed the results of barium enema examinations carried out on a total of 179 patients in whom a diagnosis of carcinoma of the colon was subsequently confirmed. During the period of the investigation a total of 12,250 barium enema studies had been made, giving an incidence of carcinoma of the colon of 1·5%.

The lesions are considered in three groups: those occurring in the caecum, those in the ascending, transverse, and descending colons, and those in the sigmoid colon. When carcinoma of the rectum was excluded there were left 130 cases of verified carcinoma, of which 109 were subjected to barium enema examination. In this group a tumour was missed on first examination in 11 instances, giving a false-negative error of about 10%.

When the groups were taken separately it was found that errors of diagnosis in carcinoma of the caecum were more frequent than at other sites; thus of 22 cases examined, the lesion was missed in 6, giving a false-negative error of 27%. In the middle part of the colon diagnostic accuracy was highest, there being only one error in 35 examinations. Of the 52 cases with lesions in the sigmoid colon examined by barium enema, a false-negative error was made in 4 (about 8%).

Many factors appear to have contributed to these errors, among them failure adequately to fill the caecum with barium, the presence of faecal contents in the caecum, and failure to empty the caecum. In the sigmoid area errors were due to incomplete demonstration of overlying loops as well as, in some cases, to the human element in failure to recognize an obvious lesion. The authors comment on the high proportion of negative findings normally yielded by the barium enema as a factor that possibly induces a lower level of alertness in the radiologist than he would display in other circumstances. They conclude that, among other things, an awareness of the inherent pitfalls of barium enema examination would tend to create a higher degree of diagnostic accuracy in this field. *A. M. Rackow*

864. **The Tomogram: Its Formation and Content.** [Monograph, in English]
P. EDHOLM. *Acta radiologica* [*Acta radiol. (Stockh.)*] Suppl. 193, 1–109, 1960. 74 figs., 35 refs.

RADIOTHERAPY

865. **The Radiotherapy of Malignant Tumours of the Eyelids.** (Le traitement roentgenthérapique des cancers palpébraux)
F. BACLESSE and M. A. DOLLFUS. *Archives d'ophtalmologie et revue générale d'ophtalmologie* [*Arch. Ophtal. (Paris)*] **20**, 473–489, July–Aug. [received Oct.], 1960. 12 figs.

This study is based on 556 cases of epithelioma of the eyelids treated at the Fondation Curie, Paris, between the years 1937 and 1953. Of these tumours, 136 of which were recurrences after other forms of treatment, 499 (90%) appeared on the lower lid or region of the medial canthus and only 57 on the upper lid or outer canthal region; 73% of the tumours were proved histologically to be basal-celled carcinomata. A complex table is presented relating the proportion of cures to each of three tumour sizes and eight different sites. At 5 years 405 cases were considered to be clinically cured, an over-all cure rate of 72·8%. Details are given of the technique, which, it is stressed, is all-important, the dosage, and methods for protection of the globe. The principal complications of treatment were lacrimal obstruction, punctate keratitis, cataract, and (rarely) iridocyclitis and glaucoma. (The authors point out that some 400 of these cases treated up to 1950 were previously reported (*J. Radiol. Électrol.*, 1958, **39**, 832; *Abstr. Wld Med.*, 1959, **26**, 191).)

[The information given in this important paper is extremely condensed and will repay study in the original.]

J. H. Dobree

866. **Malignant Effusions Treated by Colloidal Radioactive Yttrium Silicate**
J. WALTER. *British Medical Journal* [*Brit. med. J.*] **2**, 1282–1284, Oct. 29, 1960. 1 fig., 10 refs.

A new radio-isotope preparation—colloidal radioactive yttrium (^{90}Y) silicate—was tried at the Sheffield National Centre for Radiotherapy in the treatment of 15 patients with malignant pleural and peritoneal effusions,

The physical properties and the advantages of this preparation are described. The chief advantages of ^{90}Y are its high β-ray energy compared with radioactive phosphorus and radioactive gold (^{198}Au), giving a higher depth dose in tissue, and the absence of gamma radiation,

making radiation protection of the staff much easier. The amount injected varied from 21 mc. to 75 mc. in fluid volumes of 100 to 400 ml., the technique being simple and identical with that used for colloidal ^{198}Au. There were no serious side-effects or practical difficulties, and the results were comparable with those obtained with ^{198}Au. Some of the patients were in poor condition with a very bad prognosis when treatment started. Of the 15 patients in the series, 6 died within one month; in 6 of the remaining 9 " satisfactory " palliation was achieved for periods varying from 5 to 19 months.

K. E. Halnan

867. **The Functional Effect of Pulmonary Irradiation**
M. SUTTON. *British Medical Journal* [*Brit. med. J.*] **2**, 838–841, Sept. 17, 1960. 4 figs., 21 refs.

At Hammersmith Hospital, London, respiratory function was studied in patients receiving lung irradiation, either directly because of bronchial carcinoma or indirectly because of carcinoma of the breast. The patients were given conventional 240-kV. deep x-ray therapy or supervoltage radiation from the 8-MeV. linear accelerator. In all patients vital capacity, indirect maximum capacity, and standard ventilation were estimated twice before radiotherapy was begun, weekly during treatment, and thereafter at monthly intervals.

During irradiation there was definite improvement in lung function in patients with carcinoma of the lung given 8-MeV. therapy, but at the end of one year there was a moderate functional disability associated with some evidence of post-irradiation fibrosis. Patients with lung carcinoma receiving conventional therapy showed a falling-off in lung function during treatment coinciding with skin reaction and general malaise. Lung function in patients with breast carcinoma remained fairly constant throughout treatment.

M. P. Cole

868. **High Energies in Moving-field Therapy.** (Alte energie nella terapia di movimento)
F. WACHSMANN. *Radiobiologia, radioterapia e fisica medica* [*Radiobiol. Radioter. Fis. med.*] **15**, 297–303, 1960. 8 figs.

In this review from the University of Erlangen, Germany, the author points out that high-energy radiation by x rays and gamma rays has become more freely available in the past decade with the development of apparatus such as the Van de Graaff generator, linear accelerator, and betatron and radioactive cobalt units. For moving-field therapy it is superior to conventional deep therapy at 200 kV., since the beam is narrower, owing to decreased scatter, and the dosage distribution is more uniform as compared with fixed fields. The ideal now is a combination of ultra-hard rays and moving fields. He suggests there is probably no advantage in energies above 15 MeV., at which level the exit dose begins to exceed the entry dose. Several of the available models are compared; a proprietary betatron (18 MeV.) is commended especially for its easy mobility. Moving-field therapy demands high accuracy in positioning of the patient, as there is rapid fall-off in dosage outside the treated area.

Tangential pendulum therapy is valuable for superficial tumours, such as those of the breast, as it secures protection of deeper structures. Eccentric pendulum therapy is useful for treating cylindrical volumes at depth as, for example, gynaecological lesions. Moving-field electron therapy can be used for large parts of the body surface, the depth of penetration being adjustable by altering the voltage. For routine work the tele-cobalt unit is satisfactory, but the betatron is even better and also covers electron therapy. In practice, high doses are surprisingly well tolerated—better than with deep therapy. Some results from the U.S.A. are quoted to show the degree of improvement obtained, especially in the treatment of lung cancer. The author recalls the opinion expressed at a recent international radiological congress that in the course of the next decade 80% of radiotherapeutic apparatus will be of " ultra-hard " type, and he considers that it should also be of moving-field type.

J. Walter

869. **On the X-ray Treatment of Kaposi's Disease: with Case Histories.** (Sul trattamento roentgenterapico del morbo di Kaposi. Contributo casistico)
L. BARONE. *Radiobiologia, radioterapia e fisica medica* [*Radiobiol. Radioter. Fis. med.*] **15**, 304–312, 1960. Bibliography.

In this discussion of the x-ray treatment of Kaposi's disease, reported from the University of Genoa, the author points out that the disease is not sarcoma, but a hyperplastic condition of the reticulo-endothelial system. The skin is the chief site affected, but the mucosae and viscera (stomach, intestines, lung, spleen, liver, and kidney) and the bone marrow (with resulting rarefaction of bone) are involved in some 10% of cases. The aetiology is unknown. Histologically, the picture is one of newly formed blood and lymph vessels, dense infiltration of fusiform perivascular cells and to a lesser degree of round cells [? young fibroblasts], with extravasation of erythrocytes and haemosiderin; the emphasis may be on either the angiomatous or the fibroblastic process. The commonest age is 40 to 70 years, but the disease may occur in the young. X-ray therapy is the treatment of choice, the lesions being usually very radiosensitive, although an occasional resistant case may be encountered. Rapid disappearance of the lesions is the rule, with residual dark-brown pigmentation; recurrences may also be treated in the same way. Lesions in bone usually also respond, but visceral lesions are less amenable to therapy. Superficial x rays (for example, 100 kV.) usually suffice, but deep therapy at 200 kV. may be used. Ultra-soft (grenz) rays are preferred by some radiologists, while electron therapy (1 to 5 MeV.) is also useful. Small repeated doses, such as 100 r. per session, are given every few days to a total of 1,200 to 2,000 r. Radioactive isotopes have not proved useful. If treatment is successful progress of the disease may be arrested for many years. In the past decade 10 cases have been seen in the University Dermatological Clinic, Genoa. The best results are seen in the earlier cases. Radiation is considered the best of the available methods of treatment.

J. Walter